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     FILE 'REGISTRY' ENTERED AT 15:22:36 ON 22 OCT 2003
                   E CYCLOSPORIN/CN 5
L1               2 S E3
                   E ETHANOL/CN 5
L2               1 S E3
                   E PROPYLENE GLYCOL/CN 5
L3               1 S E3
L4               2 S L2 OR L3

                   E POLYOXYETHYLENE CASTOR OIL/CN 5
                   E TWEEN/CN 5
L6              41 S TWEEN ?/CN
                   E MYRJ/CN 5
L7               1 S E3
L8              42 S L6 OR L7

     FILE 'HCAPLUS' ENTERED AT 15:49:25 ON 22 OCT 2003
L1               2 SEA FILE=REGISTRY ABB=ON  PLU=ON  CYCLOSPORIN/CN
L2               1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ETHANOL/CN
L3               1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "PROPYLENE GLYCOL"/CN
L4               2 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 OR L3
L6              41 SEA FILE=REGISTRY ABB=ON  PLU=ON  TWEEN ?/CN
L7               1 SEA FILE=REGISTRY ABB=ON  PLU=ON  MYRJ/CN
L8              42 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 OR L7
L9             411 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L1 OR CYCLOSPORIN#)
                   AND (L4 OR ETHANOL OR (ET OR ETHYL)(W)(ALCOHOL OR ALC)
                   OR PROPYLENE GLYCOL OR ETOH)
L10             80 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND (L8 OR TWEEN OR
                   MYRJ OR (POLYOXYETHYLENE OR POLY(W)(OXYETHYLENE OR OXY
                   ETHYLENE) OR POLYOXY ETHYLENE)(W)CASTOR OIL)
L11             49 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND (ENCAPSUL? OR
                   CAPSUL? OR OINTMENT OR EYE DROP OR ORAL OR MOUTH OR PER
                   OS OR INJECT### OR INTRAVENOUS? OR IV  OR I V OR INTRA
                   VENOUS?)

L11  ANSWER 1 OF 49  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2003:590983  HCAPLUS
DOCUMENT NUMBER:          139:154895
TITLE:                    A process for preparation of tablets containing
                          lipophilic drugs
INVENTOR(S):              Alander, Jari; Norberg, Staffan; Hansson, Henri;
                          Svaerd, Marianne; Hovgaard, Lars
PATENT ASSIGNEE(S):       Galenica Ab, Swed.
SOURCE:                   PCT Int. Appl., 27 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
     ---------------    ----  --------      ---------------  --------
     WO 2003061627       A1   20030731      WO 2003-SE92     20030121
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
             NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ,
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TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT,
LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: SE 2002-154 A 20020121

AB A process for the preparation of a self-dispersing or self-emulsifying immediate-release tablet comprises the steps of mixing a granulation medium containing an active lipophilic substance with one or more non-swellable fillers and auxiliary components, granulation of the mixture into granules, drying and sieving granules into a size below 1 mm, mixing the granules with tableting aids, and compressing the mixture into tablets. The granulation medium is a liquid crystalline phase, an emulsion or microemulsion comprising an oil, a surfactant and a polar liquid The invention also refers to a process for the preparation of tablets from a granulation medium comprising oil and surfactant, as well as to tablets prepared by this processes. For example, tablets with **cyclosporin** A originating from soluble filler and binder were prepared using a granulation medium containing Akolip LM 23.0 g, Akoline MCM 1.0 g, **cyclosporin** A 11.0 g, and **ethanol** 22.0 g, Povidone K25 (binder) 22.0 g, and Isomalt DC 100 (filler) 154.0 g. Tablets with a total weight of 500 mg (25 mg **cyclosporin** A) and a crushing strength between 6 and 8 kp were produced. The dissoln. was slightly faster and **cyclosporin** A solved to the same extent as a com. formulation (Sandimmun Neoral 25 mg **capsule**).

IT **59865-13-3, Cyclosporin** A
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of tablets containing lipophilic drugs using liquid crystalline
phase or emulsion as granulation medium)

IT **64-17-5, Ethanol**, biological studies
9004-99-3, Myrj 52 **9005-65-6, Tween** 80
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of tablets containing lipophilic drugs using liquid crystalline
phase or emulsion as granulation medium)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:551372 HCAPLUS
DOCUMENT NUMBER: 139:106487
TITLE: Taxane based compositions containing solubilizers
INVENTOR(S): Zhang, Kai; Smith, Gregory A.
PATENT ASSIGNEE(S): Ivax Research, Inc., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057208	A1	20030717	WO 2002-US41632	20021227

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-344921P P 20011228

AB Disclosed are taxane-based compns. and methods of using the same to achieve target blood levels of a taxane in a mammal, e.g., to treat taxane-responsive malignant and non-malignant diseases. Compns. of the invention exhibit long-term stability and overall palatability. Also disclosed are methods for using the compns. as anal. tools for pharmacokinetic studies. Thus, a formulation contained paclitaxel 1.20, Vitamin E TPGS 40.00, **propylene glycol** 40.00, ascorbyl palmitate 0.50, DL-α-tocopherol 0.50, and alc. qs to 100 mL.

IT **57-55-6, Propylene glycol**, biological studies **64-17-5, Ethanol**, biological studies **9005-64-5, Tween** 20 **9005-65-6, Tween** 80 **9005-66-7, Tween** 40 **9005-67-8, Tween** 60 **9005-71-4, Tween** 65 **59865-13-3, Cyclosporin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(taxane based compns. containing solubilizers)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:511120 HCAPLUS
DOCUMENT NUMBER: 139:74040
TITLE: Pharmaceutical compositions comprising a **cyclosporin**, a hydrophilic surfactant and a lipophilic surfactant
INVENTOR(S): Sherman, Bernard Charles
PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053404	A1	20030703	WO 2002-CA1968	20021219

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,

NO, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

NZ 516269 A 20030829 NZ 2001-516269 20011220
PRIORITY APPLN. INFO.: NZ 2001-516269 A 20011220
NZ 2002-519837 A 20020628

AB Pharmaceutical compns., which enable high absorption when administered orally, comprise a **cyclosporin** or **cyclosporin** derivative dissolved in a solvent-surfactant system further comprising a hydrophilic surfactant and a lipophilic surfactant, with minimal quantities of solvents. A composition for **capsules** contained **cyclosporine** 100, **propylene glycol** 160, Polyoxyl 35 castor oil 220, sorbitan monooleate 160, and PEG 8000 20.

IT **57-55-6**, **Propylene glycol**, biological studies **57-55-6D**, **Propylene glycol**, fatty acid esters **9005-65-6**, Sorbitan monoleate
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. comprising a **cyclosporin** and hydrophilic and lipophilic surfactants)

IT **59865-13-3**, **Cyclosporin 79217-60-0**, **Cyclosporin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. comprising a **cyclosporin** and hydrophilic and lipophilic surfactants)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:511117 HCAPLUS
DOCUMENT NUMBER: 139:90450
TITLE: Formulation and dosage form for increasing **oral** bioavailability of hydrophilic macromolecules
INVENTOR(S): Dong, Liang C.; Wong, Patrick S. L.; Nguyen, Vu A.; Yum, Si-hong; Chao, Anthony C.; Daddona, Peter E.
PATENT ASSIGNEE(S): Alza Corporation, USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053401	A2	20030703	WO 2002-US41031	20021218

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,

NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-343005P P 20011219

AB The present invention includes a formulation and dosage form for enhancing the bioavailability of orally administered hydrophilic macromols. The formulation of the present invention includes a permeation enhancer, a hydrophilic macromol., and a carrier that exhibits in-situ gelling properties, such as nonionic surfactant. The formulation of the present invention is delivered within the GI tract as a liquid having at least some affinity for the surface of the GI mucosal membrane. Once released, it is believed that the liquid formulation spreads across one or more areas of the surface of the GI mucosal membrane, where the carrier of the formulation then transitions into a bioadhesive gel in-situ. As a bioadhesive gel, the formulation of the present invention present the hydrophilic macromol. and the permeation enhancer at the surface of the GI mucosal membrane at concns. sufficient to increase absorption of the hydrophilic macromol. through the GI mucosal membrane over a period of time. The dosage form of the present invention incorporates the formulation of the present invention and may be designed to provide the controlled release of the formulation within the GI tract over a desired period of time. Examples are give for the rheol. properties of Cremophor EL as a carrier and the bioavailability of pentosan polysulfate sodium.

IT **57-55-6, Propylene glycol**, biological studies **9005-64-5, Tween** 20 **9005-65-6, Tween** 80 **9005-66-7, Tween** 40 **9005-67-8, Tween** 60 **9005-70-3, Tween** 85 **9005-71-4, Tween** 65
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulation and dosage form for increasing **oral** bioavailability of hydrophilic macromols.)

IT **59865-13-3, Cyclosporine**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulation and dosage form for increasing **oral** bioavailability of hydrophilic macromols.)

L11 ANSWER 5 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:491019 HCAPLUS
DOCUMENT NUMBER: 139:57937
TITLE: Pharmaceutical composition comprising an oil/water/oil double microemulsion incorporated into a solid support
INVENTOR(S): Carli, Fabio; Chiellini, Elisabetta
PATENT ASSIGNEE(S): Remedia S.R.L., Italy
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003051334	A2	20030626	WO 2002-EP14472	20021218

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IT 2001-MI2694 A 20011219

AB Pharamaceutical compns. in the form of powders or microgranules, comprise an oil/water/oil double microemulsion incorporated into a solid support constituted by a microporous inorg. compound or by an adsorbent inorg. colloidal material or by a cross-linked water-swellable polymer. Thus, an emulsion contained **cyclosporin** 2.89, Akoline 0.96, water 2.69, **Tween** -80 1.05, and Akoline 29.69 g.

IT **64-17-5**, **Ethanol**, biological studies
9005-65-6, **Tween** 80 **79217-60-0**,
Cyclosporin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition comprising oil/water/oil double microemulsions incorporated into solid support)

L11 ANSWER 6 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:146486 HCAPLUS
DOCUMENT NUMBER: 138:158889
TITLE: **Cyclosporine oral** preparations
INVENTOR(S): Takahashi, Masato; Goto, Masahiro; Endo, Takahiro
PATENT ASSIGNEE(S): Toyo Capsule Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003055254	A2	20030226	JP 2001-247736	20010817

PRIORITY APPLN. INFO.: JP 2001-247736 20010817

AB The title prepns., preferably in the forms of soft **capsules** or hard **capsules**, comprise (1) 1 part **cyclosporine**, (2) 0.5-3 parts **propylene glycol**, (3) 0.5-3 parts **propylene glycol** mono- or diesters with fatty acids, (4) 1-10 parts polyoxyethylene sorbitan fatty acid esters and/or polyglycerin fatty acid esters, and (5) 0.5-10 parts viscosity modifiers selected from the group consisting of medium-chain triglycerides, plant oils, polyethylene glycol, polyvinylpyrrolidone, carboxyvinyl polymer, and polyvinyl alc. For example, a **capsule** contained **cyclosporine** 50,

propylene glycol 25, **propylene glycol** fatty acid esters 2.5, Polysorbate-80 150, and medium-chain triglyceride 140 mg.

IT **57-55-6D, Propylene glycol**, fatty acid esters **9005-65-6**, Polysorbate-80 **59865-13-3**, **Cyclosporin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**capsules** containing **cyclosporine** and solubilizers and viscosity modifiers)

L11 ANSWER 7 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:220399 HCAPLUS
DOCUMENT NUMBER: 136:252504
TITLE: Self-emulsifiable formulation having enhanced bioabsorption and immunosuppressant activities
INVENTOR(S): Chakravorty, Saibal; Bharti, Prasad
PATENT ASSIGNEE(S): RPG Life Sciences Limited, India
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022158	A1	20020321	WO 2000-IN91	20000918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001025459	A5	20020326	AU 2001-25459	20000918
BR 2000013813	A	20020430	BR 2000-13813	20000918
EP 1333851	A1	20030813	EP 2000-988993	20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: WO 2000-IN91 A 20000918

AB A self-emulsifiable formulation comprises a lipophilic system consisting of medium-chain triglycerides of caprylic acid and capric acid, and Labrasol, wherein the Labrasol also serves as a surfactant, which is combined with other selected surfactants, like Cremophor RH 40 and/or Polysorbate 80. The formulation also comprises an immunosuppressant, e.g., **cyclosporine**, hydrophilic agent preferably **EtOH**, antioxidant such as α-tocopherol and preservative e.g., benzyl alc. The formulation is prepared by dissolving the immunosuppressant in a hydrophilic agent followed by entrapment with a lipophilic agent and subsequent treatment with surfactants, preservatives and antioxidants, and is filled in a soft-gelatin shell capable of rupture in <10 min to deliver the formulation into the upper part of gastrointestinal tract, wherein it forms thermodynamically stable oil-in-water microemulsions. The formulation has enhanced

bioavailability and bioabsorption of the immunosuppressant. Thus, a formulation contained **cyclosporin** 10.00, **EtOH** 11.88, Labrasol 25.21, Polysorbate-80 25.61, Crodamol GTCC 40.00, and α-tocopherol 0.0009%.

IT **59865-13-3, Cyclosporin** A
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(self-emulsifiable formulation having enhanced bioabsorption and immunosuppressant activities)

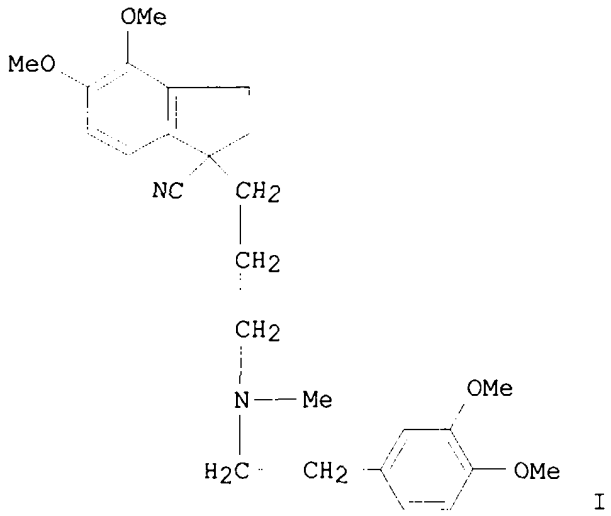
IT **57-55-6,** 1,2-**Propylene glycol,** biological studies **64-17-5, Ethanol,** biological studies **9005-65-6,** Polysorbate 80
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(self-emulsifiable formulation having enhanced bioabsorption and immunosuppressant activities)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:142508 HCAPLUS
DOCUMENT NUMBER: 136:205397
TITLE: **Oral** drug composition containing a verapamil derivative as a drug-absorption promotor
INVENTOR(S): Woo, Jong Soo; Yoo, Sung Eun
PATENT ASSIGNEE(S): Hanmi Pharm. Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002013815	A1	20020221	WO 2001-KR1096	20010627
W: AU, CA, CN, CZ, HU, IN, MX, NZ, RU, SI, YU				
EP 1184034	A2	20020306	EP 2001-111018	20010508
EP 1184034	A3	20021113		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2002049158	A1	20020425	US 2001-854051	20010511
AU 2001066399	A5	20020225	AU 2001-66399	20010627
JP 2002080399	A2	20020319	JP 2001-207750	20010709
PRIORITY APPLN. INFO.:			KR 2000-46643 A	20000811
			WO 2001-KR1096 W	20010627

OTHER SOURCE(S): MARPAT 136:205397
GI



I

AB The bioavailability of a drug which is not readily absorbed in the digestive tract can be greatly enhanced by administering an **oral** composition comprising a drug and a verapamil derivative which does not cause any adverse side effects. **Capsules** were prepared containing paclitaxel, dimethylisosorbide, Cremophor EL, **Tween** 80, α-tocopheryl acetate, erythorbic acid, and I.

IT **57-55-6**, **Propylene glycol**, biological studies **57-55-6D**, **Propylene glycol**, fatty acid esters **64-17-5**, **Ethanol**, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**oral** drug composition containing verapamil derivative as drug-absorption promoter)

IT **59865-13-3**, **Cyclosporin** a
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**oral** drug composition containing verapamil derivative as drug-absorption promoter)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:89795 HCAPLUS
DOCUMENT NUMBER: 136:139843
TITLE: Method of regulating hair growth using metal complexes of oxidized carbohydrates
INVENTOR(S): Gardlik, John Michael; Severynse-Stevens, Diana; Comstock, Bryan Gabriel
PATENT ASSIGNEE(S): The Procter & Gamble Company, USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002007685	A2	20020131	WO 2001-US23424	20010725

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002035070	A1	20020321	US 2001-909441	20010719

PRIORITY APPLN. INFO.: US 2000-220755P P 20000726

AB A method for regulating the growth of hair comprising administering to a mammal, an effective amount of a composition comprising: (a) about 0.001-99.9%, by weight, of at least one metal complex of an oxidized carbohydrate, wherein the metal complex of an oxidized carbohydrate is neither zinc gluconate nor manganese gluconate; and (b) about 0.1-99.999%, by weight, of a vehicle. The composition is administered orally, parenterally, or topically. For example, a topical composition contained zinc lactobionate 5.0%, zinc gluconate 1.0%, zinc pyrithione 1.0%, **Tween** 20 1.0%, **propylene glycol** 10.0%, dimethylisosorbide 18.0%, **EtOH** 30.0%, and water and minors up to 100%. Also, tablets were prepared containing zinc lactobionate 100 mg, Crospovidone 15 mg, lactose 200 mg, microcryst. cellulose 80 mg, and magnesium stearate 5 mg.

IT **57-55-6, Propylene glycol**, biological studies **64-17-5, Ethanol**, biological studies **79217-60-0, Cyclosporin**
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. containing metal complexes of oxidized carbohydrates for regulating hair growth)

L11 ANSWER 10 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:762786 HCAPLUS
DOCUMENT NUMBER: 135:322724
TITLE: Solid pharmaceutical compositions containing surfactants and solubilizers
INVENTOR(S): Ambuehl, Michael; Haeberlin, Barbara; Lueckel, Barbara; Meinzer, Armin; Lambert, Olivier; Marchal, Laurent
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001076561 A2 20011018 WO 2001-EP4051 20010409
WO 2001076561 A3 20020221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
FR 2807658 A1 20011019 FR 2001-4713 20010406
EP 1272163 A2 20030108 EP 2001-923719 20010409
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
BR 2001009931 A 20030527 BR 2001-9931 20010409
JP 2003530340 T2 20031014 JP 2001-574079 20010409
US 2003133984 A1 20030717 US 2002-239456 20020923
PRIORITY APPLN. INFO.: GB 2000-8785 A 20000410
WO 2001-EP4051 W 20010409

AB The present invention provides a pharmaceutical composition in a solid form comprising a poorly water-soluble drug, a solubilizing component, and a surfactant which is a semisolid or solid. The poorly soluble drug can be a **cyclosporine** or a macrolide. Thus, a composition contained **cyclosporin** A 7.7, oleyl alc. 30.8, and sodium lauryl sulfate 61.5% by weight

IT **57-55-6D, Propylene glycol**, esters with fatty acids **9004-99-3, Myrj** 52
59865-13-3, Cyclosporin A
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid pharmaceutical compns. containing solubilizers and surfactants)

L11 ANSWER 11 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:507513 HCAPLUS
DOCUMENT NUMBER: 135:97475
TITLE: Pharmaceutical formulations for the delivery of drugs having low aqueous solubility
INVENTOR(S): Unger, Evan C.; Romanowski, Marek J.
PATENT ASSIGNEE(S): ImaRx Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001049268	A1	20010712	WO 2000-US35322	20001221
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1246608	A1	20021009	EP 2000-988371	20001221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				

JP 2003520210 T2 20030702 JP 2001-549636 20001221
PRIORITY APPLN. INFO.: US 2000-478124 A 20000105
US 2000-703484 A 20001031
WO 2000-US35322 W 20001221

AB Pharmaceutical formulations are provided that increase the systemic bioavailability of a drug that has low aqueous solubility The drug is phys. entrapped by a spatially stabilized matrix of a hydrophilic polymer, but is not covalently bound thereto. Phospholipid moieties are optionally conjugated to the hydrophilic polymer, and free phospholipids, stabilizing agents and/or other excipients may be incorporated into the formulations as well. Therapeutic methods are also provided, wherein a formulation of the invention is administered to a patient to treat a condition, disorder or disease that is responsive to a particular drug. Generally, administration is **oral** or parenteral.

IT **64-17-5, Ethanol**, biological studies
9005-65-6, Tween 80 **59865-13-3, Cyclosporin** A
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrophilic polymer matrix containing stabilizers for delivery of drugs having low aqueous solubility)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:338320 HCAPLUS
DOCUMENT NUMBER: 134:344599
TITLE: **Cyclosporin** formulation containing glycerides
INVENTOR(S): Hamied, Yusuf Khwaja; Nayak, Vinay G.; Malhotra, Geena
PATENT ASSIGNEE(S): Cipla Limited, India
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032142	A1	20010510	WO 2000-GB4143	20001027
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2001032143	A1	20010510	WO 1999-IN62	19991102
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM,				

TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

GB 2362573	A1	20011128	GB 2000-12816		20000525
EP 1227793	A1	20020807	EP 2000-971598		20001027

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.:	WO 1999-IN62	A	19991102
	GB 2000-12816	A	20000525
	WO 2000-GB4143	W	20001027

AB A pharmaceutical composition in the form of a preconc. mixed either with a liquid hydrophilic phase to form a stable oil-in-water microemulsion or with a solid carrier to form a stable, solid blend of carrier and preconc., comprises a) a water-insol. pharmaceutically active material; b) one or more **propylene glycol** esters of a fatty acid; c) surfactant; and either d) a hydrophilic phase, wherein component (a) has been wholly directly dissolved in component (b) and component (b) is dispersed as tiny particles in component (d); or e) a solid carrier. The composition is substantially free from **ethanol**. A composition contained **cyclosporin** 25, glyceryl monolinoleate 17.25, **propylene glycol** monocaprylate 17.25, Cremophor EL 50.00, colloidal silica 52.50, and crospovidone 13.00 mg/**capsule**.

IT **9005-64-5**, Polyoxyethylene sorbitan monolaurate
9005-65-6, Polyoxyethylene sorbitan monooleate
9005-66-7, Polyoxyethylene sorbitan monopalmitate
9005-67-8, Polyoxyethylene sorbitan monostearate
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**cyclosporin** formulation containing glycerides)

IT **59865-13-3**, **Cyclosporin** A **79217-50-0**, **Cyclosporin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**cyclosporin** formulation containing glycerides)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER:	2001:326244 HCAPLUS
DOCUMENT NUMBER:	134:344585
TITLE:	**Oral cyclosporine** microemulsion concentrates
INVENTOR(S):	Takahashi, Masato; Goto, Masahiro
PATENT ASSIGNEE(S):	Toyo Capsule K. K., Japan
SOURCE:	Jpn. Kokai Tokkyo Koho, 3 pp. CODEN: JKXXAF
DOCUMENT TYPE:	Patent
LANGUAGE:	Japanese
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001122779	A2	20010508	JP 1999-303222	19991026
PRIORITY APPLN. INFO.:			JP 1999-303222	19991026

AB The concs. contain **cyclosporine** (I) 1, **propylene glycol** 1-3, Polysorbate 2-10, and extenders/viscosity regulators 0.5-5 weight parts. A soft **capsule** contained I 50, **propylene glycol** 50, Polysorbate 80 200, and medium-chain fatty acid triglyceride 150 mg. I was completely released from the **capsule** in H2O in 30 min.

IT **57-55-6**, **Propylene glycol**, biological studies **9005-65-6**, Polysorbate 80 **59865-13-3**, **Cyclosporine**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**oral cyclosporine** microemulsion concs.)

L11 ANSWER 14 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:228688 HCAPLUS
DOCUMENT NUMBER: 134:271250
TITLE: Surface modified particulate pharmaceutical compositions containing surfactants
INVENTOR(S): Pace, Gary W.; Mishra, Awadhesh K.; Snow, Robert A.
PATENT ASSIGNEE(S): RTP Pharma Inc., USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021154	A2	20010329	WO 2000-US25880	20000921
WO 2001021154	A3	20011025		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1214059	A2	20020619	EP 2000-970467	20000921
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003509453	T2	20030311	JP 2001-524580	20000921

PRIORITY APPLN. INFO.: US 1999-154964P P 19990921
WO 2000-US25880 W 20000921

AB This invention disclosure relates to compns. for the delivery of stable surface modified sub-micron and micron sized particles of water-insol. drugs from a non-aqueous medium that self-disperses on exposure to an aqueous environment. Thus, compns. of **cyclosporine** that self-disperse into surface-modified micron- or sub-micron-sized particle suspensions contained **cyclosporine** 50, Epax 4510-TG 150, vitamin E-TPGS 45, **Tween** 80 405, and **EtOH** 150 mg.

IT **57-55-6D**, **Propylene glycol**, fatty acid esters **64-17-5**, **Ethanol**, biological studies **9005-64-5**, **Tween** 20 **9005-65-6**,

Tween 80 **9005-66-7, Tween** 40
9005-67-8, Tween 60 **9005-70-3,**
Tween 85 **59865-13-3D, Cyclosporin,**
derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surface modified particulate pharmaceutical compns. containing surfactants)

L11 ANSWER 15 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:31306 HCAPLUS
DOCUMENT NUMBER: 134:105846
TITLE: Clear aqueous dispersions of triglycerides and surfactants for delivery of drugs and nutrients
INVENTOR(S): Chen, Feng-Jing; Patel, Mahesh V.
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001001960	A1	20010111	WO 2000-US15133	20000602
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6267985	B1	20010731	US 1999-345615	19990630
EP 1194120	A1	20020410	EP 2000-938039	20000602
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003503440	T2	20030128	JP 2001-507455	20000602

PRIORITY APPLN. INFO.: US 1999-345615 A 19990630
WO 2000-US15133 W 20000602

AB The present invention relates to drug and nutrient delivery systems, and in particular to pharmaceutical compns. and methods for improved solubilization of triglycerides and improved delivery of therapeutic agents. Compns. of the present invention include a triglyceride and a carrier, where the carrier is formed from a combination of at least two surfactants, at least one of which is hydrophilic. Upon dilution with an aqueous solvent, the composition forms a clear, aqueous dispersion of the triglyceride and surfactants. An optional therapeutic agent can be incorporated into the composition, or can be co-administered with the composition The invention also provides methods of enhancing triglyceride solubility and methods of treatment with therapeutic agents using these compns. Several formulations were presented of compns. that can be prepared according to the present invention using a variety of therapeutic agents. Examples of aqueous dispersions include: (1) Cremophor RH-40 0.75, Peceol 0.25, corn oil 0.40, and fenofibrate 0.10; (2) Cremophor RH-40 0.57, Crovol M-40 0.43, corn

oil 0.40, and Rofecoxib 0.15; (3) **Tween** 80 0.70, **Tween** 85 0.35, Miglyol 812 0.30, Paclitaxel 0.10, and PEG 400 0.25; or (4) Kessco PEG 400 MO 0.33, corn oil 0.30, and Terbinafine 0.25 parts, resp.

IT **57-55-6, Propylene glycol**, biological studies **57-55-6D, Propylene glycol**, esters and ethers **64-17-5, Ethanol**, biological studies **9004-99-3**, Polyethylene glycol stearate **9005-64-5**, Polysorbate 20 **9005-65-6**, Polysorbate 80 **9005-66-7, Tween** 40 **9005-67-8, Tween** 60 **9005-70-3, Tween** 85 **59865-13-3, Cyclosporin** A
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clear aqueous dispersions of triglyceride and surfactants for delivery of drugs and nutrients)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 16 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:911036 HCAPLUS
DOCUMENT NUMBER: 134:76383
TITLE: **Oral** pharmaceutical compositions containing taxanes
INVENTOR(S): Gutierrez-Rocca, Jose C.; Cacace, Janice L.; Selim, Sami; Testman, Robert; Rutledge, J. Michael
PATENT ASSIGNEE(S): Baker Norton Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078247	A1	20001228	WO 1999-US13821	19990618
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9946955	A1	20010109	AU 1999-46955	19990618
BR 9917403	A	20020709	BR 1999-17403	19990618
EP 1221908	A1	20020717	EP 1999-930408	19990618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, RO, CY				
JP 2003502349	T2	20030121	JP 2001-504316	19990618

PRIORITY APPLN. INFO.: WO 1999-US13821 A 19990618

AB Pharmaceutical compns. for **oral** administration to mammalian subjects comprise a taxane or taxane derivative (e.g., paclitaxel or docetaxel) as active ingredient and a vehicle comprising at least 30% by weight of a carrier for the taxane, the

carrier having an HLB value of at least about 10. The compns. may also comprise 0-70% of a viscosity-reducing co-solubilizer. The compns. may be incorporated into conventional **oral** pharmaceutical dosage forms, or can be in the form of a 2-part drug wherein the first part includes the taxane in a solubilizing vehicle and the second part comprises a carrier for the taxane to promote **oral** absorption. Methods of treatment of taxane-responsive disease conditions employing the novel compns. are also disclosed, whereby the compns. can be administered alone or in association with an **oral** bioavailability enhancing agent. A formulation containing **Tween** 80 at 18 mg/kg and paclitaxel gave an absolute bioavailability of 54% which was >15% for **i.v.** drug.

IT **57-55-6, Propylene glycol**, biological studies **64-17-5, Ethanol**, biological studies **9004-99-3, Myrj** 49 **9005-65-6, Tween** 80 **9005-66-7, Tween** 40 **9005-67-8, Tween** 60 **9005-71-4, Tween** 65 **59865-13-3, Cyclosporin** A
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**oral** pharmaceuticals containing taxanes)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 17 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:861507 HCAPLUS
DOCUMENT NUMBER: 134:21479
TITLE: **Capsule** compositions containing **cyclosporin** and surfactants
INVENTOR(S): Ambuhl, Michael; Luckel, Barbara; Haberlin, Barbara; Meinzer, Armin
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000072867	A2	20001207	WO 2000-EP4829	20000526
WO 2000072867	A3	20010405		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000011030	A	20020226	BR 2000-11030	20000526
EP 1181035	A2	20020227	EP 2000-943742	20000526
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

GB 2367004	A1	20020327	GB 2001-28277	20000526
DE 10084671	T	20020606	DE 2000-10084671	20000526
US 2002068083	A1	20020606	US 2000-579372	20000526
US 6432445	B1	20020813		
DE 20022951	U1	20020926	DE 2000-20022951	20000526
JP 2003500454	T2	20030107	JP 2000-620976	20000526
NZ 515154	A	20030829	NZ 2000-515154	20000526
ZA 2001009658	A	20020820	ZA 2001-9658	20011123
NO 2001005785	A	20020123	NO 2001-5785	20011127
US 2002188134	A1	20021212	US 2002-217732	20020813

PRIORITY APPLN. INFO.:
GB 1999-12476 A 19990528
US 2000-579372 A1 20000526
WO 2000-EP4829 W 20000526

AB This invention provides a **capsule** composition comprising a **cyclosporin** and a carrier medium containing surfactants such as ethoxylated hydrogenated castor oil and **EtOH**. Thus, a composition was made up with the following components: Cremophor EL 56, Miglyol-812 16, Span-80 8, and **cyclosporin** A 10, and **EtOH** 10%.

IT **64-17-5, Ethanol**, biological studies
9005-65-6, Tween 80 **59865-13-3, Cyclosporin 79217-60-0, Cyclosporin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**capsule** compns. containing **cyclosporin** and surfactants)

L11 ANSWER 18 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:814284 HCAPLUS
DOCUMENT NUMBER: 133:366419
TITLE: Lipid particles on the basis of mixtures of liquid and solid lipids and method for producing same for drug delivery
INVENTOR(S): Muller, Rainer Helmut; Jenning, Volkhard; Mader, Karsten; Lippacher, Andreas
PATENT ASSIGNEE(S): Pharmasol G.m.b.H., Germany
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000067728	A2	20001116	WO 2000-EP4112	20000508
WO 2000067728	A3	20010809		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19938371	A1	20010222	DE 1999-19938371	19990809
DE 19945203	A1	20001221	DE 1999-19945203	19990921
EP 1176949	A2	20020206	EP 2000-931138	20000508

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

BR 2000010354	A	20020305	BR 2000-10354	20000508
JP 2002544155	T2	20021224	JP 2000-616755	20000508
ZA 2001008794	A	20020715	ZA 2001-8794	20011025

PRIORITY APPLN. INFO.:

DE 1999-19921034	A	19990507
DE 1999-19938371	A	19990809
DE 1999-19945203	A	19990921
DE 2000-10016357	A	20000331
WO 2000-EP4112	W	20000508

AB The invention relates to lipid particles which do or do not carry active agents and comprise a mixed matrix consisting of solid and liquid lipid (so-called solid/liquid particles). The inventive particles are provided with a disordered structure (semicryst., mostly non-crystalline to amorphous) in the semisolid to solid condition. The invention also relates to a method for producing said dispersions and especially a method for producing highly concentrated lipid particle dispersions with a lipid content of 30 % to 95 % or a solids content of 30 % to 95 % (lipid and stabilizer). Said dispersions are integral particles unlike the biamphiphilic creams and/or the highly concentrated particle dispersions result in free-flowing particle dispersions when diluted with the outer phase.

IT **64-17-5, Ethanol,** biological studies
9005-65-6, Tween 80 **79217-60-0, Cyclosporin**
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid particles on the basis of mixts. of liquid and solid lipids and method for producing same for drug delivery)

L11 ANSWER 19 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:608551 HCAPLUS
DOCUMENT NUMBER: 133:213151
TITLE: Pharmaceutical compositions and methods for improved delivery of hydrophobic therapeutic agents
INVENTOR(S): Patel, Manesh V.; Chen, Feng-Jing
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050007	A1	20000831	WO 2000-US165	20000105

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6294192	B1	20010925	US 1999-258654	19990226
NZ 513810	A	20010928	NZ 2000-513810	20000105
EP 1158959	A1	20011205	EP 2000-901394	20000105
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002537317	T2	20021105	JP 2000-600619	20000105

PRIORITY APPLN. INFO.: US 1999-258654 A 19990226
WO 2000-US165 W 20000105

AB The present invention relates to triglyceride-free pharmaceutical compns. for delivery of hydrophobic therapeutic agents. Compns. of the present invention include a hydrophobic therapeutic agent and a carrier, where the carrier is formed from a combination of a hydrophilic surfactant and a hydrophobic surfactant. Upon dilution with an aqueous solvent, the composition forms a clear, aqueous dispersion of the surfactants containing the therapeutic agent. The invention also provides methods of treatment with hydrophobic therapeutic agents using these compns. A pharmaceutical composition contained **cyclosporin** 0.14, Cremophor RH-40 0.41, Arlacel186 0.29, sodium taurocholate 0.26, and **propylene glycol** 0.46 mg.

IT **57-55-6**, 1,2-Propanediol, biological studies
57-55-6D, **Propylene glycol**, ethers
64-17-5, **Ethanol**, biological studies
9004-99-3, Polyoxyethylene stearate **9005-64-5**, **Tween** 20 **9005-65-6**, Polysorbate 80
9005-66-7, **Tween** 40 **9005-67-8**, **Tween** 60 **59865-13-3**, **Cyclosporine**
79217-60-0, **Cyclosporin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical compns. and methods for improved delivery of hydrophobic therapeutic agents)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 20 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:585399 HCAPLUS
DOCUMENT NUMBER: 133:168409
TITLE: Ciclosporin soft **capsules** with good drug bioavailability
INVENTOR(S): Takahashi, Masato; Goto, Masahiro
PATENT ASSIGNEE(S): Toyo Capsule K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000229878	A2	20000822	JP 1999-29462	19990208

PRIORITY APPLN. INFO.: JP 1999-29462 19990208

AB Soft **capsules** contain 1 weight part ciclosporin (I) dissolved in solns. comprising 1-3 weight parts **propylene glycol** (II), 2-4 weight parts polyglycerin monofatty acid esters, and excipients and/or viscosity-adjusting agents. Soft

capsules containing I 50, II 100, decaglyceryl monolaurate 150, decaglyceryl trioleate 50, and middle-chain triglyceride 30 mg released 100% I within 30 min in artificial intestinal juice.

IT **59865-13-3**, Ciclosporin
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(ciclosporin soft **capsules** with good drug bioavailability)

IT **57-55-6**, **Propylene glycol**, biological studies **9005-65-6**, Polysorbate 80
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in ciclosporin soft **capsules** with good drug bioavailability)

L11 ANSWER 21 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:442138 HCAPLUS
DOCUMENT NUMBER: 133:64013
TITLE: **Cyclosporin** solution
INVENTOR(S): Fischer, Wilfried
PATENT ASSIGNEE(S): Ratiopharm G.m.b.H., Germany
SOURCE: *Ger. Offen.*, 7 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19859910	A1	20000629	DE 1998-19859910	19981223
DE 19859910	C2	20010322		
WO 2000038702	A1	20000706	WO 1999-EP10358	19991223
W: AU, CA, CZ, HU, JP, NO, PL, RU, SK, US, ZA				
RW: *AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,* NL, PT, SE				
EP 1140135	A1	20011010	EP 1999-964670	19991223
EP 1140135	B1	20030917		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002533401	T2	20021008	JP 2000-590654	19991223
AU 762963	B2	20030710	AU 2000-30434	19991223
NO 2001002932	A	20010613	NO 2001-2932	20010613
ZA 2001004828	A	20020913	ZA 2001-4828	20010613

PRIORITY APPLN. INFO.: DE 1998-19859910 A 19981223
WO 1999-EP10358 W 19991223

AB Colloidal solns. of **cyclosporin** in water, which can be *diluted with water in any proportion, are prepared by use of* dexpanthenol as solubilizer in combination with an anionic surfactant and ≥1 nonionic surfactant. Thus, a solution of **cyclosporin** A 100 in **EtOH** 150 mg was combined with a clear solution comprising dexpanthenol 100, SDS (anionic surfactant) 50, polysorbate 80 (nonionic surfactant) 100, and PEG glyceryl stearate (nonionic surfactant) 400 mg and the mixture was placed in a gelatin **capsule**. After **oral** administration of 1 **capsule** to beagle dogs, the mean blood level of **cyclosporin** after 1.5 h was 1398.17 ng/mL.

IT **59865-13-3**, **Cyclosporin** A

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**cyclosporin** solution)

IT **9005-65-6,** Polysorbate 80
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**cyclosporin** solution)

IT **79217-60-0, Cyclosporin**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(solution)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 22 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:388867 HCAPLUS
DOCUMENT NUMBER: 133:22451
TITLE: **Cyclosporin capsules**
INVENTOR(S): Takahashi, Masato; Goto, Masahiro
PATENT ASSIGNEE(S): Toyo Capsule K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000159660	A2	20000613	JP 1998-347822	19981120

PRIORITY APPLN. INFO.: JP 1998-347822 19981120

AB **Cyclosporin capsules** are prepared by dissolving **cyclosporins** in sorbitan sesquioleate-POE sorbitan oleate mixture, mixing with medium-chain fatty acid triglyceride or **propylene glycol** medium-chain fatty acid esters and filling into **capsules.**

IT **57-55-6D, Propylene glycol,** medium-chain fatty acid esters **9005-65-6,** Polyoxyethylene sorbitan oleate **59865-13-3, Cyclosporin** **79217-60-0, Cyclosporin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**cyclosporin capsules**)

L11 ANSWER 23 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:14983 HCAPLUS
DOCUMENT NUMBER: 132:83650
TITLE: Solid dispersed preparation of poorly water-soluble drug containing oil, fatty acid or mixtures thereof
INVENTOR(S): Lee, Beom Jin
PATENT ASSIGNEE(S): Won Jin Biopharma Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000179	A1	20000106	WO 1999-KR341	19990628
W: AU, CA, CN, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
KR 2000006503	A	20000125	KR 1999-24437	19990626
AU 9946556	A1	20000117	AU 1999-46556	19990628

PRIORITY APPLN. INFO.: KR 1998-24563 A 19980627
KR 1999-24437 A 19990626
WO 1999-KR341 W 19990628

AB Disclosed is a solid dispersed preparation for poorly water-soluble drugs, which is prepared by dissolving or dispersing the poorly water-soluble drugs in an oil, a fatty acid or a mixture thereof, mixing the solution or dispersion in a water-soluble polyol matrix and drying the mixture The solid dispersed preparation can be formulated into a power formulation or a granule formulation. The solid dispersed preparation is improved in the solubility of poorly water-soluble drugs in the gastro-intestinal tract, resulting in a great increase in the bioavailability of the drugs. In addition, the solid dispersed preparation gives the pharmaceutical solns. to the problems that the conventional semi-solid or liquid prepns. possess, enabling medicinally effective, poorly water-soluble compds. to be formulated, molded and processed, quickly and in an economically favorable manner without use of any organic solvent. Examples are given for emulsions containing mixts. of waxes, oils, and aqueous phase.

IT **57-55-6**, **Propylene glycol**, biological studies **9004-99-3**, Polyethylene glycol stearate **9005-65-6**, Polysorbate 80 **9005-67-8D**, Polysorbate 60, esters **59865-13-3**, **Cyclosporin** A
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid dispersed preparation of poorly water-soluble drug containing oils and fatty acid or mixts.)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 24 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:818248 HCAPLUS
DOCUMENT NUMBER: 132:54881
TITLE: Hydrophilic binary systems for the administration of lipophilic compounds
INVENTOR(S): Al-Razzak, Laman A.; Constantinides, Panayiotis Pericleous; Kaul, Dilip; Lipari, John M.; McChesney-Harris, Lisa L.; Abdullah, Bashar Y.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: U.S., 7 pp., Cont.-in-part of U.S. Ser. No. 816375, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6008192	A	19991228	US 1998-41881	19980312
PRIORITY APPLN. INFO.:			US 1997-816375 B2	19970312

AB Binary pharmaceutical compns. comprise (i) a **cyclosporin**, (ii) a hydrophilic phase and (iii) a surfactant provide bioavailability of the active ingredient which is equivalent to that provided by ternary compns., but without the need for a lipophilic phase. A composition was prepared containing **cyclosporin** A 10, Cremophor EL 40 % weight/vil. and **propylene glycol** to 100 mL.

IT **57-55-6**, 1,2-Propanediol, biological studies **64-17-5**, **Ethanol**, biological studies **9004-99-3**, **Myrj** 52 **9005-65-6**, **Tween** 80
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrophilic binary systems for the administration of lipophilic compds.)

IT **59865-13-3**, **Cyclosporin** A
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrophilic binary systems for the administration of lipophilic compds.)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 25 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:633257 HCAPLUS
DOCUMENT NUMBER: 131:262618
TITLE: **Oral cyclosporin** formulations
INVENTOR(S): Cho, Moo J.; Levy, Ralph E.; Pouletty, Philippe J.
PATENT ASSIGNEE(S): Sangstat Medical Corporation, USA; University of North Carolina At Chapel Hill
SOURCE: U.S., 12 pp., Cont.-in-part of U.S. 5,766,629. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5962019	A	19991005	US 1997-956841	19971023
US 5834017	A	19981110	US 1995-519689	19950825
US 5766629	A	19980616	US 1996-620021	19960321
WO 9920296	A1	19990429	WO 1998-US22330	19981021

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,

CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9898106	A1	19990510	AU 1998-98106	19981021
EP 956035	A1	19991117	EP 1998-952393	19981021
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9806271	A	20000404	BR 1998-6271	19981021
JP 2000516267	T2	20001205	JP 1999-524568	19981021
NZ 336253	A	20010629	NZ 1998-336253	19981021
RU 2174405	C2	20011010	RU 1999-113343	19981021
ZA 9809684	A	19990425	ZA 1998-9684	19981023
NO 9903096	A	19990817	NO 1999-3096	19990622
AU 764599	B2	20030821	AU 1999-63033	19991202
AU 9963033	A1	20000217		

PRIORITY APPLN. INFO.:	US 1995-519689	A2	19950825
	US 1996-620021	A2	19960321
	AU 1996-66441	A	19960731
	US 1997-956841	A	19971023
	WO 1998-US22330	W	19981021

AB Improved **oral cyclosporin** formulations which have high bioavailability and are capable of administration in both liquid and hard **capsule** form are provided. In the subject formulations, **cyclosporin** is delivered in an orally acceptable vehicle comprising ≥1 C2-3 alkanol solvent in combination with ≥1 nonionic surfactant. The subject formulations may further comprise at least one cosolvent, where cosolvents of interest include fatty acids and diols. The subject formulations find use in immunosuppressive therapy.

IT **59865-13-3, Cyclosporin**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**oral** compns. with improved bioavailability containing **cyclosporin** and alkanol solvents and nonionic surfactants)

IT **64-17-5, Ethanol,** biological studies
9005-65-6, Polyoxyethylene sorbitan monooleate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**oral** compns. with improved bioavailability containing **cyclosporin** and alkanol solvents and nonionic surfactants)

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 26 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER:	1999:390372 HCAPLUS
DOCUMENT NUMBER:	131:35884
TITLE:	Pharmaceutical compositions containing an omega-3 fatty acid oil
INVENTOR(S):	Mishra, Awadhesh K.; Ramtoola, Zeibunnissa; Moussa, Iskandar; Clarke, Nuala M.
PATENT ASSIGNEE(S):	Severson, Mary L., USA; Cyclosporine Therapeutics Limited
SOURCE:	PCT Int. Appl., 44 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9929316	A1	19990617	WO 1998-US26329	19981210
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2313024	AA	19990617	CA 1998-2313024	19981210
AU 9918174	A1	19990628	AU 1999-18174	19981210
AU 743098	B2	20020117		
EP 1039893	A1	20001004	EP 1998-963070	19981210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6284268	B1	20010904	US 1998-209066	19981210
JP 2001525363	T2	20011211	JP 2000-523987	19981210
NO 2000002991	A	20000809	NO 2000-2991	20000609

PRIORITY APPLN. INFO.:	US 1997-988270	A	19971210
	US 1998-84516P	P	19980507
	WO 1998-US26329	W	19981210

AB Self-emulsifying microemulsion or emulsion preconc. pharmaceutical compns. containing an omega-3 fatty acid oil such as a fish oil and a poorly water soluble therapeutic agent, such as **cyclosporin**, are formulated for administration, particularly **oral** administration, to a human. The preconcs., which are substantially free of or contain only minor amts. of a hydrophilic solvent system, contain a pharmaceutically effective amount of (1) an omega-3 fatty acid oil, (2) a therapeutically effective amount of a poorly water soluble therapeutic agent that is substantially soluble in the omega-3 fatty acid oil, and (3) a surfactant system comprising at least one surfactant. Microemulsions or emulsions formed by diluting the self-emulsifying preconc. with an aqueous solution are also provided. A microemulsion preconc. containing ω-3 fatty acid oil K85EE 37% (405 mg), a surfactant system comprising Cremophor RH 40-**Tween** 80 (2:1) 53% (583 mg) and Labrasol 10% (110 mg) was used for preparation of soft **capsule** containing **cyclosporin** A 100 mg.

IT **57-55-6**, 1,2-Propanediol, biological studies **64-17-5**, **Ethanol**, biological studies **9004-99-3**, **Myrj** 52 **9005-64-5**, **Tween** 20 **9005-65-6**, **Tween** 80 **59865-13-3**, **Cyclosporin** A **79217-60-0**, **Cyclosporin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical emulsion or microemulsion preconcs. containing ω-3 fatty acid oil and surfactants)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 27 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:296978 HCAPLUS
DOCUMENT NUMBER: 130:357158

TITLE: **Cyclosporin** soft **capsules**
INVENTOR(S): Takahashi, Masato
PATENT ASSIGNEE(S): Toyo Capsule K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11124339	A2	19990511	JP 1997-304917	19971020
PRIORITY APPLN. INFO.:			JP 1997-304917	19971020

AB A liquid carrier for **cyclosporin** formulated in soft **capsules**, comprises a blend of polyglycerin fatty acid esters with vegetable oil or a blend of polyglycerin fatty acid esters with polyethylene glycol and/or **propylene glycol**. The formulation further comprises nonionic surfactants, e.g. polyoxyethylene sorbitan monooleate and sorbitan sesquioleate. A formulation containing **cyclosporin** 1, decaglyceryl trioleate (HLB 7) 1, and medium-chain triglycerides 8 parts was filled into gelatin **capsules**.

IT **57-55-6**, **Propylene glycol**, biological studies **9005-65-6**, Polyoxyethylene sorbitan monooleate **59865-13-3**, **Cyclosporin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid carriers for **cyclosporin** soft **capsules**)

L11 ANSWER 28 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:282113 HCAPLUS
DOCUMENT NUMBER: 130:316653
TITLE: **Oral cyclosporin** formulations
INVENTOR(S): Chu, Moo J.; Levy, Ralph E.; Pouletty, Philippe J.
PATENT ASSIGNEE(S): Sangstat Medical Corporation, USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920296	A1	19990429	WO 1998-US22330	19981021
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 5962019	A	19991005	US 1997-956841	19971023
AU 9898106	A1	19990510	AU 1998-98106	19981021

EP 956035	A1	19991117	EP 1998-952393		19981021
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
BR 9806271	A	20000404	BR 1998-6271		19981021
JP 2000516267	T2	20001205	JP 1999-524568		19981021
NZ 336253	A	20010629	NZ 1998-336253		19981021
RU 2174405	C2	20011010	RU 1999-113343		19981021
NO 9903096	A	19990817	NO 1999-3096		19990622
PRIORITY APPLN. INFO.:			US 1997-956841	A	19971023
			US 1995-519689	A2	19950825
			US 1996-620021	A2	19960321
			WO 1998-US22330	W	19981021

AB Improved **oral cyclosporin** formulations which have high bioavailability and are capable of administration in both liquid and hard **capsule** form are provided. In the subject formulations, **cyclosporin** is delivered in an orally acceptable vehicle comprising at least one alkanol solvent of from 2 to 3 carbon atoms in combination with at least one nonionic surfactant. The subject formulations may further comprise at least one cosolvent, where cosolvents of interest include fatty acids and diols. The subject formulations find use in immuno-suppressive therapy. An **oral** solution contained **cyclosporin** A 100 mg, **ethanol** 0.1 mL, **Tween** 80 300 mg, and iso-Pr myristate q.s. to 1 mL.

IT **57-55-6, Propylene glycol**, biological studies **64-17-5, Ethanol**, biological studies **9005-65-6**, Polyoxyethylene monosorbitan monooleate **59865-13-3, Cyclosporin** A
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**oral cyclosporin** compns. containing alkanol and polyglycol and nonionic surfactants)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 29 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:113534 HCAPLUS
DOCUMENT NUMBER: 130:187182
TITLE: Self-emulsifying formulation for lipophilic compounds
INVENTOR(S): Morozowich, Walter; Gao, Ping
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906024	A1	19990211	WO 1998-US14818	19980727
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9885739	A1	19990222	AU 1998-85739	19980727
AU 728698	B2	20010118		
EP 999826	A1	20000517	EP 1998-936889	19980727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9811058	A	20000905	BR 1998-11058	19980727
JP 2002511099	T2	20020409	JP 1999-510974	19980727
NZ 502569	A	20020531	NZ 1998-502569	19980727
RU 2211021	C2	20030827	RU 2000-104856	19980727
FI 2000000170	A	20000128	FI 2000-170	20000128
NO 2000000467	A	20000329	NO 2000-467	20000128
US 2003044434	A1	20030306	US 2002-224742	20020821

PRIORITY APPLN. INFO.:
US 1997-54012P P 19970729
US 1997-54078P P 19970729
US 1998-122926 A3 19980727
WO 1998-US14818 W 19980727

AB A novel pharmaceutical composition comprises a particular oil phase which contains a lipophilic drug, a mixture of C16-22 diglyceride and monoglyceride in a ratio of 9:1 to about 6:4 by weight (diglyceride:monoglyceride), 1 or more solvent, and 1 or more surfactant. The composition is a self-emulsifying formulation which provides high concentration and high **oral** bioavailability for lipophilic compds. Thus, a formulation contained a pyranone derivative 26.4, **EtOH/propylene glycol** (1:1) 17.3 diolein/monoolein (8:2) 22.7, Cremophor RH40 26.9, ethanolamine 5.3, and SLS 1.4%.

IT **57-55-6**, 1,2-Propanediol, biological studies **64-17-5**, **Ethanol**, biological studies **9004-99-3**, PEG stearate **59865-13-3**, **Cyclosporin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(self-emulsifying formulation for lipophilic drugs containing glycerides)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 30 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:621129 HCAPLUS
DOCUMENT NUMBER: 129:235663
TITLE: Hydrophilic binary systems for the administration of **cyclosporin**
INVENTOR(S): Al-Razzak, Laman A.; Constantinides, Panayiotis Pericleous; Kaul, Dilip; Lipari, John M.; Mcchesney-Harris, Lisa L.; Abdullah, Bashar Y.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840094	A1	19980917	WO 1998-US4927	19980312

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9864618	A1	19980929	AU 1998-64618	19980312
EP 969856	A1	20000112	EP 1998-910361	19980312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO				
BR 9808656	A	20000523	BR 1998-8656	19980312
NZ 337316	A	20010629	NZ 1998-337316	19980312
JP 2001516351	T2	20010925	JP 1998-539828	19980312
SK 282714	B6	20021106	SK 1999-1199	19980312
NO 9904266	A	19991110	NO 1999-4266	19990902
MX 9908342	A	20000228	MX 1999-8342	19990910
PRIORITY APPLN. INFO.:			US 1997-816375 A	19970312
			WO 1998-US4927 W	19980312

AB Binary pharmaceutical compns. comprising (1) a **cyclosporin** compound, (2) a hydrophilic phase and (3) a surfactant, provide bioavailability of the active ingredient which is equivalent to that provided by ternary compns., but without the need for a lipophilic phase. A composition contained **cyclosporin** A 10, Cremophor EL 40, and **propylene glycol** q.s. 100 mL. The **oral** bioavailability of 5 mg/kg of composition was evaluated in dogs. The Cmax, Tmax, and AUC was 1010 ng/mL, 1.0 h, and 5916.5 ng/h/mL, resp.

IT **59865-13-3, Cyclosporine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrophilic binary systems for administration of **cyclosporin**)

IT **57-55-6, Propylene glycol**, biological studies **64-17-5, Ethanol**, biological studies **9004-99-3, Myrj** 52 **9005-65-6, Tween** 80
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrophilic binary systems for administration of **cyclosporin**)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 31 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:621098 HCAPLUS
DOCUMENT NUMBER: 129:250219
TITLE: Lipophilic binary systems for the administration of lipophilic compounds
INVENTOR(S): Al-Razzak, Laman A.; Constantinides, Panayiotis Pericleous; Gao, Rong; Kaul, Dilip; Lipari, John M.; Mazer, Terrence B.; McChesney-Harris, Lisa L.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 21 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840051	A1	19980917	WO 1998-US4899	19980312
W: CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 973502	A1	20000126	EP 1998-909159	19980312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001515491	T2	20010918	JP 1998-539817	19980312
MX 9908337	A	20000228	MX 1999-8337	19990910

PRIORITY APPLN. INFO.: US 1997-820392 A 19970312
WO 1998-US4899 W 19980312

AB Binary pharmaceutical formulations comprising (1) a **cyclosporine** compound, (2) a lipophilic phase, and (3) a surfactant provide bioavailability of the active ingredient which is equivalent to that provided by ternary compns., but without the need for a hydrophilic phase. A composition containing **cyclosporin** A 10, **Tween**-80 25, and Miglyol 812 q.s. to 100 % (weight/volume) was filled into **capsules** and delivered to dogs at a dose of 5 mg/kg to study drug bioavailability.

IT **57-55-6D**, **Propylene glycol**, C8-10 alkyl esters **9005-65-6**, **Tween** 80
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipophilic binary systems to improve bioavailability of **cyclosporine**)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 32 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:414633 HCAPLUS
DOCUMENT NUMBER: 129:58829
TITLE: **Oral cyclosporin** formulations comprising C2-3 alkanols and nonionic surfactants
INVENTOR(S): Cho, Moo J.; Levy, Ralph E.; Pouletty, Philippe J.
PATENT ASSIGNEE(S): Sangstat Medical Corporation, USA
SOURCE: U.S., 11 pp., Cont.-in-part of U.S. Ser. No. 519,689.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5766629	A	19980616	US 1996-620021	19960321
US 5834017	A	19981110	US 1995-519689	19950825
CA 2202887	AA	19970306	CA 1996-2202887	19960731

WO 9707787		A1	19970306	WO 1996-US12569	19960731
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
AU 9666441		A1	19970319	AU 1996-66441	19960731
AU 709548		B2	19990902		
EP 789561		A1	19970820	EP 1996-926214	19960731
R:	AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9606603		A	19970930	BR 1996-6603	19960731
CN 1164828		A	19971112	CN 1996-190962	19960731
JP 3009742		B2	20000214	JP 1997-510271	19960731
JP 10509462		T2	19980914		
NZ 313899		A	20000327	NZ 1996-313899	19960731
RU 2172183		C2	20010820	RU 1997-107086	19960731
NZ 502344		A	20010928	NZ 1996-502344	19960731
TW 460287		B	20011021	TW 1996-85111622	19960923
WO 9734622		A1	19970925	WO 1997-US305	19970110
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9715312		A1	19971010	AU 1997-15312	19970110
ZA 9701569		A	19980108	ZA 1997-1569	19970224
NO 9701890		A	19970424	NO 1997-1890	19970424
BG 62875		B1	20001031	BG 1997-101443	19970425
US 5962019		A	19991005	US 1997-956841	19971023
US 6254885		B1	20010703	US 1998-37176	19980309
AU 764599		B2	20030821	AU 1999-63033	19991202
AU 9963033		A1	20000217		

PRIORITY APPLN. INFO.:	US 1995-519689	A2	19950825
	US 1996-620021	A	19960321
	US 1996-622516	A	19960325
	AU 1996-66441	A	19960731
	NZ 1996-313899	A1	19960731
	WO 1996-US12569	W	19960731
	WO 1997-US305	W	19970110

AB Improved **oral cyclosporin** formulations which have high bioavailability and are capable of administration in hard **capsules** are provided. In the formulations, **cyclosporin** is delivered in an orally acceptable vehicle comprising at least one alkanol solvent of from 2 to 3 carbon atoms in combination with at least one non-ionic surfactant. The formulations may further comprise at least one cosolvent, where cosolvents of interest include fatty acids and diols. The formulations find use in immuno-suppressive therapy. An **oral cyclosporin** solution contained **Tween** 80 300 mg, **ethanol** 0.1, and iso-Pr myristate q.s. 1.0 mL.

IT **59865-13-3, Cyclosporin** a **79217-60-0, Cyclosporin**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**oral cyclosporin** formulations comprising C2-3 alkanols and nonionic surfactants)

IT **64-17-5, Ethanol**, biological studies
9005-65-6, Tween 80
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**oral cyclosporin** formulations comprising C2-3 alkanols and nonionic surfactants)

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 33 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:207280 HCAPLUS
DOCUMENT NUMBER: 128:275101
TITLE: Gas and gaseous precursor filled microspheres as topical and subcutaneous delivery vehicles
INVENTOR(S): Unger, Evan C.; Matsunaga, Terry O.; Yellowhair, David
PATENT ASSIGNEE(S): Imarx Pharmaceutical Corp., USA
SOURCE: U.S., 40 pp., Cont.-in-part of U.S. Ser. No. 307,305.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 19
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5733572	A	19980331	US 1994-346426	19941129
US 5088499	A	19920218	US 1990-569828	19900820
WO 9109629	A1	19910711	WO 1990-US7500	19901219
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AT 180170	E	19990615	AT 1991-902857	19901219
ES 2131051	T3	19990716	ES 1991-902857	19901219
JP 3309356	B2	20020729	JP 1991-503276	19901219
JP 05502675	T2	19930513		
US 5228446	A	19930720	US 1991-717084	19910618
WO 9222247	A1	19921223	WO 1992-US2615	19920331
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU 9220020	A1	19930112	AU 1992-20020	19920331
AU 667471	B2	19960328		
JP 06508364	T2	19940922	JP 1993-500847	19920331
JP 3456584	B2	20031014		
EP 616508	A1	19940928	EP 1992-912456	19920331
EP 616508	B1	20010718		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
EP 660687	A1	19950705	EP 1992-912455	19920331
EP 660687	B1	19981028		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
AT 172625	E	19981115	AT 1992-912455	19920331
ES 2124733	T3	19990216	ES 1992-912455	19920331
JP 3053217	B2	20000619	JP 1993-500845	19920331

AT 203148	E	20010815	AT 1992-912456	19920331
ES 2159280	T3	20011001	ES 1992-912456	19920331
US 5469854	A	19951128	US 1993-76239	19930611
US 5580575	A	19961203	US 1993-76250	19930611
US 5348016	A	19940920	US 1993-88268	19930707
US 5542935	A	19960806	US 1993-160232	19931130
US 5585112	A	19961217	US 1993-159687	19931130
US 5769080	A	19980623	US 1994-199462	19940222
WO 9428874	A1	19941222	WO 1994-US5633	19940519
W: AU, CA, CN, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5773024	A	19980630	US 1994-307305	19940916
CA 2177713	AA	19950608	CA 1994-2177713	19941130
WO 9515118	A1	19950608	WO 1994-US13817	19941130
W: AU, CA, CN, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 740528	A1	19961106	EP 1995-908414	19941130
EP 740528	B1	20030326		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09506098	T2	19970617	JP 1995-515763	19941130
AT 235228	E	20030415	AT 1995-908414	19941130
US 5571497	A	19961105	US 1995-468056	19950606
CN 1180310	A	19980429	CN 1996-193069	19960327
CN 1102045	B	20030226		
US 6001335	A	19991214	US 1996-665719	19960618
US 5935553	A	19990810	US 1996-758179	19961125
US 5985246	A	19991116	US 1997-888426	19970708
AU 9856271	A1	19980507	AU 1998-56271	19980224
AU 713127	B2	19991125		
AU 9888405	A1	19981203	AU 1998-88405	19981012
AU 731072	B2	20010322		
HK 1013625	A1	20000420	HK 1998-114978	19981223
AU 9910043	A1	19990304	AU 1999-10043	19990104

PRIORITY APPLN. INFO.:

US 1989-455707	B2	19891222
US 1990-569828	A2	19900820
US 1991-716899	B2	19910618
US 1991-717084	A2	19910618
US 1993-76239	A2	19930611
US 1993-76250	A2	19930611
US 1993-159674	B2	19931130
US 1993-159687	A2	19931130
US 1993-160232	A2	19931130
US 1994-307305	A2	19940916
WO 1990-US7500	W	19901219
US 1991-716793	A	19910618
US 1991-750877	A3	19910826
US 1992-818069	A3	19920108
WO 1992-US2610	W	19920331
WO 1992-US2615	A	19920331
US 1992-967974	A3	19921027
US 1993-17683	A3	19930212
US 1993-18112	B3	19930217
US 1993-85608	A3	19930630
US 1993-88268	A3	19930707
US 1993-163039	A3	19931206

US	1994-212553	B2 19940311
AU	1994-70416	A3 19940519
US	1994-346426	A 19941129
AU	1995-21850	A3 19941130
WO	1994-US13817	W 19941130
US	1995-395683	A3 19950228
US	1995-468056	A3 19950606
US	1995-471250	A3 19950606
US	1996-665719	A3 19960618

AB Gas and gaseous precursor filled microspheres, and foams provide novel topical and s.c. delivery vehicles for various active ingredients, including drugs and cosmetics. Gas and gaseous precursor filled microcapsules were prepared from dipalmitoylphosphatidylcholine.

IT **57-55-6**, 1,2-Propanediol, biological studies **64-17-5**, **Ethanol**, biological studies **9004-99-3**, Polyoxyethylene stearate **9005-64-5**, Polysorbate 20 **9005-65-6**, Polysorbate 80 **9005-66-7**, Polysorbate 40 **9005-67-8**, Polysorbate 60 **79217-60-0**, **Cyclosporin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gas and gaseous precursor filled microspheres as topical and s.c. delivery vehicles)

REFERENCE COUNT: 314 THERE ARE 314 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 34 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:150231 HCAPLUS
DOCUMENT NUMBER: 128:158918
TITLE: Water-soluble (hydrophilic) excipients for difficultly soluble drugs
INVENTOR(S): Zhou, Dehe
PATENT ASSIGNEE(S): Zhou, Dehe, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 5 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1144695	A	19970312	CN 1996-107550	19960529
CN 1104258	B	20030402		

PRIORITY APPLN. INFO.: CN 1996-107550 19960529

AB Water-soluble (hydrophilic) excipients for difficultly soluble drugs contain nonionic solubilizers and alcs. with/without antioxidants.

IT **64-17-5**, **Ethanol**, biological studies **9005-64-5**, **Tween** 20 **59865-13-3**, **Cyclosporin** A
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(water-soluble (hydrophilic) excipients for difficultly soluble drugs)

L11 ANSWER 35 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:38655 HCAPLUS
DOCUMENT NUMBER: 128:93221

TITLE: **Cyclosporin** soft **capsules** having glycerin-free gelatin film
INVENTOR(S): Woo, Jong Soo
PATENT ASSIGNEE(S): Hanmi Pharmaceutical Co., Ltd., S. Korea
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10007550	A2	19980113	JP 1996-227156	19960828
JP 2855135	B2	19990210		
EP 813876	A1	19971229	EP 1997-109152	19970605
EP 813876	B1	20020327		
R: BE, DE, FR, GB, IT, SI, LT, LV, RO				
AT 214937	E	20020415	AT 1997-109152	19970605
ES 2175217	T3	20021116	ES 1997-109152	19970605
CA 2240705	AA	19971224	CA 1997-2240705	19970619
AU 9733411	A1	19980107	AU 1997-33411	19970619
AU 719251	B2	20000504		
EP 869810	A1	19981014	EP 1997-929227	19970619
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1207044	A	19990203	CN 1997-191060	19970619
ZA 9705448	A	19990319	ZA 1997-5448	19970619
BR 9706804	A	19991103	BR 1997-6804	19970619
JP 2000505480	T2	20000509	JP 1998-502297	19970619
IL 123676	A1	20020210	IL 1997-123676	19970619
RU 2181055	C2	20020410	RU 1998-105629	19970619
SK 283216	B6	20030304	SK 1998-371	19970619
NO 9801200	A	19980317	NO 1998-1200	19980317
NO 9802382	A	19980526	NO 1998-2382	19980526
JP 2923503	B2	19990726	JP 1998-194739	19980709
JP 11100326	A2	19990413		
AU 753018	B2	20021003	AU 2000-43820	20000703

PRIORITY APPLN. INFO.:
KR 1996-22417 A 19960619
JP 1996-227156 A3 19960828
KR 1997-8750 A 19970314
CA 1997-2226091 A3 19970619
WO 1997-EP3213 W 19970619

AB The soft **capsules** having gelatin film containing polyethylene glycol (I) and **propylene glycol** (II) as plasticizers contain (1) **cyclosporin** (III), (2) hydrophilic I, nonhydrophilic propylene carbonate, or their mixture as cosurfactant, (3) a mixture of alkanol fatty acid esters, medium-chain triglycerides, and fatty acid monoglycerides, and (4) surfactants with HLB 8-17. The **capsules** are manufactured by mixing (2), (3), and (4), dissolving III to the mixture under heating, **encapsulating** the resulting concentrated liquid with a gelatin film containing I and II using a soft **capsule** filler, and air cooling in a cooling drum. The soft **capsules** show good storage stability, and high drug bioavailability. A soft **capsule** containing III 25, I 45, propylene carbonate 25, polyoxyethylene hydrogenated castor oil 35, polyoxyethylene sorbitan monolaurate 85, Et linoleate 40, caprylic acid/capric acid

triglyceride 5, and oleic acid monoglyceride 35 mg in a gelatin film containing I and II was prepared The **capsule** content was stable in its appearance over 30 days since no glycerin was used, while a control **capsule** using gelatin film containing glycerin gave precipitation after 5 days.

IT **59865-13-3, Cyclosporin A 79217-60-0, Cyclosporin**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**cyclosporin** soft **capsules** having glycerin-free gelatin film and containing specific surfactants and oil compns.)

IT **57-55-6**, 1,2-Propanediol, biological studies
9005-64-5, Polyoxyethylene sorbitan monolaurate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**cyclosporin** soft **capsules** having glycerin-free gelatin film and containing specific surfactants and oil compns.)

L11 ANSWER 36 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:262353 HCAPLUS
DOCUMENT NUMBER: 126:242906
TITLE: **Oral cyclosporin** formulations
INVENTOR(S): Cho, Moo J.; Levy, Ralph E.; Pouletty, Philippe J.; Floc, H. Robert; Merle, Christian
PATENT ASSIGNEE(S): Sangstat Medical Corporation, USA; University of North Carolina At Chapel Hill
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9707787	A1	19970306	WO 1996-US12569	19960731
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 5834017	A	19981110	US 1995-519689	19950825
US 5766629	A	19980616	US 1996-620021	19960321
US 5827822	A	19981027	US 1996-622516	19960325
AU 9666441	A1	19970319	AU 1996-66441	19960731
AU 709548	B2	19990902		
EP 789561	A1	19970820	EP 1996-926214	19960731
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9606603	A	19970930	BR 1996-6603	19960731
JP 3009742	B2	20000214	JP 1997-510271	19960731
JP 10509462	T2	19980914		
NZ 313899	A	20000327	NZ 1996-313899	19960731

RU 2172183	C2	20010820	RU 1997-107086	19960731	
WO 9735603	A1	19971002	WO 1997-US4627	19970321	
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9722190	A1	19971017	AU 1997-22190	19970321	
ZA 9702560	A	19971017	ZA 1997-2560	19970325	
NO 9701890	A	19970424	NO 1997-1890	19970424	
BG 62875	B1	20001031	BG 1997-101443	19970425	
US 2002016290	A1	20020207	US 1998-113532	19980710	
AU 764599	B2	20030821	AU 1999-63033	19991202	
AU 9963033	A1	20000217			

PRIORITY APPLN. INFO.:	US 1995-519689	A	19950825
	US 1996-620021	A	19960321
	US 1996-622516	A	19960325
	AU 1996-66441	A	19960731
	WO 1996-US12569	W	19960731
	WO 1997-US4627	W	19970321

AB Improved **oral cyclosporin** formulations which have high bioavailability and are capable of administration in hard **capsules** of nanoparticles are provided. In the subject formulation, **cyclosporin** in delivered in an orally acceptable vehicle comprising at least one alkanol solvent of 2-3 carbons in combination with at least one nonionic surfactant. The subject formulations may further comprise at least one cosolvent, where cosolvents of interest include fatty acids and diols. The subject formulations find use in immuno-suppressive therapy. For example, 5 g of **cyclosporin** A was added to 5 mL of **ethanol** and to the resulting solution 15 g of Polysorbate 80 was added and the volume was completed to 50 mL by a mixture of **propylene glycol** and polyethylene glycol 400. The mixture was sufficiently stirred at room temperature until a homogeneous solution was formed.

IT **57-55-6, Propylene glycol**, biological studies **64-17-5, Ethanol**, biological studies **9005-65-6**, Polyoxyethylene monosorbitan monooleate **59865-13-3, Cyclosporin** A
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**oral cyclosporin** formulations for immunosuppressive therapy)

L11 ANSWER 37 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER:	1997:251016 HCAPLUS
DOCUMENT NUMBER:	126:242887
TITLE:	Oil-in-water microemulsions
INVENTOR(S):	Hamied, Y. K.; Nayak, V. G.; Malhotra, G.
PATENT ASSIGNEE(S):	Cipla Limited, India
SOURCE:	Eur. Pat. Appl., 11 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 760237	A1	19970305	EP 1995-306022	19950830
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
ZA 9607034	A	19970220	ZA 1996-7034	19960819
AU 9662162	A1	19970306	AU 1996-62162	19960820
AU 706995	B2	19990701		
US 5929030	A	19990727	US 1996-697204	19960821

PRIORITY APPLN. INFO.: EP 1995-306022 A 19950830

AB Water-insol. pharmaceutically active substances such as **cyclosporin** are formulated for administration in the form of an oil-in-water microemulsion, wherein the active substance is fully dissolved in the dispersed oil particles. The oil is C8 to C20 fatty acid vegetable oil glycerides, and lecithin and another surfactant are included to form and stabilize the microemulsion in which the hydrophilic phase comprises **propylene glycol**. A preconc. comprising the above components but free from any hydrophilic phase can be utilised to make up the compns., which are most suitably soft gelatine **capsules** or **oral** administration fluids. The glycerides are preferably from castor oil, coconut oil or peanut oil.

IT **9005-64-5**, Polyoxyethylene sorbitan monolaurate
9005-65-6, Polyoxyethylene sorbitan monooleate
9005-66-7, Polyoxyethylene sorbitan monopalmitate
9005-67-8, Polyoxyethylene sorbitan monostearate
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oil-in-water microemulsions)

IT **59865-13-3**, **Cyclosporin** A
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oil-in-water microemulsions)

L11 ANSWER 38 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:34732 HCAPLUS
DOCUMENT NUMBER: 126:135606
TITLE: **Cyclosporin**-containing soft **capsule** compositions
INVENTOR(S): Woo, Jong S.
PATENT ASSIGNEE(S): Hanmi Pharm. Ind. Co., Ltd., S. Korea
SOURCE: U.S., 12 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5589455	A	19961231	US 1995-427187	19950421

PRIORITY APPLN. INFO.: KR 1994-37948 19941228

AB The present invention relates to a soft **capsule** composition containing a stable microemulsion concentrate which is more stable and suitable for the preparation of **cyclosporin**-containing soft **capsules**. More specifically, the present invention relates to a microemulsion concentrate containing **cyclosporin** as an active ingredient, polyethylene glycol as a cosurfactant, one component or a mixture of two or more selected from the group consisting of an

esterified compound of fatty acid and primary alc., medium chain fatty acid triglyceride and monoglyceride as an oil component, and a surfactant having HLB value of 10 to 17 such as Nikkol HCO-50 or **Tween** 20, which is suitable for formulation into soft **capsules** and to a soft **capsule** composition containing said microemulsion concentrate In the microemulsion concentrate according to the present invention, **cyclosporin**, polyethylene glycol, the oil component and the surfactant are present in the ratio of 1:0.1-10:1-10:1-10, preferably 1:0.5-8:2-6:2-8, by weight The soft **capsule** preparation containing polyethylene glycol, Et linoleate, caprylic/capric acid triglyceride, oleic acid monoglyceride, Nikkol HCO-50 or **Tween** 20 according to the present invention is highly stable during storage in comparison with the prior soft **capsules** containing **ethanol**, **propylene glycol**, transcutol, glycofurol, etc., as a cosurfactant, and provides an advantage in that the appearance and composition content of the soft **capsule** are not changed, and further that since the bioavailability of **cyclosporin** is about 4 times or more as high as that of the prior com. products and pharmacokinetic properties of **cyclosporin** including difference between bioavailabilities in resp. subjects are improved, the administration dosage, side effects and costs of the drugs are reduced.

IT **9005-64-5, Tween** 20 **9005-65-6, Tween** 80 **9005-66-7, Tween** 40 **9005-67-8, Tween** 60 **59865-13-3, Cyclosporin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**cyclosporin**-containing soft **capsule** compns.)

L11 ANSWER 39 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:879034 HCAPLUS
DOCUMENT NUMBER: 123:266139
TITLE: **Cyclosporin**-containing powder composition
INVENTOR(S): Kim, Jung Woo; Shin, Hee Jong; Park, Joon Kyu; Min, Kyeong Bok
PATENT ASSIGNEE(S): Chong Kun Dang Corp., S. Korea
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9522982	A1	19950831	WO 1994-KR125	19940916
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2161343	AA	19950831	CA 1994-2161343	19940916
AU 9477091	A1	19950911	AU 1994-77091	19940916
EP 702562	A1	19960327	EP 1994-927847	19940916
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, PT				
CN 1121694	A	19960501	CN 1994-191895	19940916

JP 09501701	T2	19970218	JP 1994-522269	19940916
US 5543393	A	19960806	US 1994-347137	19941123
FI 9505042	A	19951129	FI 1995-5042	19951023
NO 9504245	A	19951222	NO 1995-4245	19951024
PRIORITY APPLN. INFO.:			KR 1994-3490	19940225
			WO 1994-KR125	19940916

AB A powder composition with improved stability and an increased bioavailability comprises **cyclosporin**, a nonionic hydrophilic surfactant, and a porous carrier. The powder is prepared by dissolving **cyclosporin** and a surfactant in an organic solvent, adding a porous carrier to the resulting solution and evaporating the organic solvent from the mixture Solutol HS15 500 was dissolved in 1000 mg of **EtOH** and then 100 mg of **cyclosporin** was dissolved therein. The resulting solution was mixed with 500 mg of sorbitol and the mixture was dried at 40° under reduced pressure to evaporate **EtOH**.

IT **64-17-5, Ethanol**, biological studies
9004-99-3, Myrj 52 **9005-65-6, Tween** 80 **59865-13-3, Cyclosporin** A **79217-60-0D, Cyclosporin**, derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(powder compns. for **cyclosporin** containing nonionic surfactant and porous carrier)

L11 ANSWER 40 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:753643 HCAPLUS
DOCUMENT NUMBER: 123:152922
TITLE: Transparent liquid for **encapsulated** drug delivery
INVENTOR(S): Yiv, Seang H.
PATENT ASSIGNEE(S): Ibah, Inc., USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9514037	A1	19950526	WO 1994-US13394	19941116
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2176927	AA	19950526	CA 1994-2176927	19941116
AU 9512917	A1	19950606	AU 1995-12917	19941116
AU 692506	B2	19980611		
EP 736041	A1	19961009	EP 1995-904099	19941116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09510182	T2	19971014	JP 1994-514649	19941116
US 5707648	A	19980113	US 1995-406935	19950517
PRIORITY APPLN. INFO.:			US 1993-153846	19931117
			WO 1994-US13394	19941116

AB A stable transparent multi-component composition useful for the delivery of water soluble active agents to animals is provided. The compns. are formulated with a mixture of an oil phase, an aqueous phase, and a surfactant system, along with the active agent to be delivered to the animal. The compns. are specially formulated to be compatible with **capsules** such as gelatin and starch **capsules** . The aqueous phase of the compns. contains a substantial amount of polyethylene glycol and can optionally also contain a plasticizer. Preferred active agents are proteinaceous materials. Calcein bioavailability from a transparent liquid containing Captex 200 12, Imwitor 308 29.8, **Tween** 80 19.2, PEG 400 32.4, sorbitol 1.6, water 3% weight/weight, and 100 mM calcein solution in 10 mM Tris pH 7.4 3% weight/weight, resp., was studied.

IT **9005-65-6**, **Tween** 80 **59865-13-3**, **Cyclosporin** A
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (transparent liquid compns. for **encapsulated** drug delivery)

L11 ANSWER 41 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:589583 HCAPLUS
DOCUMENT NUMBER: 122:322530
TITLE: **Cyclosporin** soft **capsules** containing dimethylisosorbide and surfactants
INVENTOR(S): Woo, Jong Soo
PATENT ASSIGNEE(S): Hanmi Pharm. Ind. Co., Ltd., S. Korea
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 650721	A1	19950503	EP 1994-110184	19940630
EP 650721	B1	20000913		
R: BE, DE, FR, GB, IT				
CN 1097597	A	19950125	CN 1994-106301	19940530
CN 1077800	B	20020116		
JP 08157358	A2	19960618	JP 1994-151149	19940701

PRIORITY APPLN. INFO.: KR 1993-12291 A 19930701

AB A microemulsion concentrate containing **cyclosporin** as an active ingredient, dimethylisosorbide as a cosurfactant, an oil, and a surfactant in the ratio of 1:1-5:1-5:2-10 is used for the formulation of a soft **capsule** for **oral** administration. Since dimethylisosorbide has substantially no membrane permeation property, the soft **capsule** preparation according to the present invention is outstandingly stable in comparison with the soft **capsules** containing **ethanol** as a cosurfactant in the prior art. A soft gelatin **capsule** contained **cyclosporin** 25, dimethylisosorbide 45, Labrafil M 1944 CS 75, **Tween** 80 5, and refined fish oil 115 mg. The bioavailability of **capsules** of the invention in rabbits and humans was similar to the bioavailability of **ethanol**-containing **capsules**.

IT **9005-65-6**, **Tween** 80 **59865-13-3**,

Cyclosporin a
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**cyclosporin** soft **capsules** containing
dimethylisosorbide and surfactants)

L11 ANSWER 42 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:341141 HCAPLUS
DOCUMENT NUMBER: 122:114973
TITLE: Pharmaceutical preparation containing a poorly soluble drug with improved bioavailability
INVENTOR(S): Posanski, Ulrich
PATENT ASSIGNEE(S): Galenik Labor Freiburg GmbH, Germany
SOURCE: Ger. Offen., 5 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4322826	A1	19950112	DE 1993-4322826	19930708
CA 2164100	AA	19950119	CA 1994-2164100	19940708
WO 9501785	A1	19950119	WO 1994-EP2238	19940708
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
WO 9501786	A1	19950119	WO 1994-EP2248	19940708
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9473457	A1	19950206	AU 1994-73457	19940708
AU 689486	B2	19980402		
AU 9473850	A1	19950206	AU 1994-73850	19940708
EP 710103	A1	19960508	EP 1994-922269	19940708
EP 710103	B1	20010613		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
EP 710104	A1	19960508	EP 1994-923715	19940708
EP 710104	B1	19981104		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
HU 73427	A2	19960729	HU 1995-3868	19940708
CN 1128495	A	19960807	CN 1994-192714	19940708
CN 1121853	B	20030924		
BR 9407002	A	19960903	BR 1994-7002	19940708
HU 73661	A2	19960930	HU 1995-3965	19940708
JP 08512301	T2	19961224	JP 1994-503830	19940708
JP 08512303	T2	19961224	JP 1994-503833	19940708
AT 172876	E	19981115	AT 1994-923715	19940708

ES 2124420	T3	19990201	ES 1994-923715	19940708
RU 2140291	C1	19991027	RU 1996-102012	19940708
SK 280615	B6	20000516	SK 1996-19	19940708
PL 179717	B1	20001031	PL 1994-312255	19940708
EP 1092429	A1	20010418	EP 2000-122248	19940708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI				
ES 2159564	T3	20011016	ES 1994-922269	19940708
CZ 291401	B6	20030312	CZ 1996-45	19940708
FI 9600032	A	19960209	FI 1996-32	19960103
FI 9600042	A	19960104	FI 1996-42	19960104
NO 9600062	A	19960105	NO 1996-62	19960105
NO 9600069	A	19960105	NO 1996-69	19960105
US 2002099067	A1	20020725	US 2002-40842	20020107

PRIORITY APPLN. INFO.:

DE 1993-4322826	A	19930708
EP 1994-922269	A3	19940708
WO 1994-EP2238	W	19940708
WO 1994-EP2248	W	19940708
US 1996-578527	B1	19960105
US 1998-97915	B1	19980617
US 2000-524965	A1	20000314

AB The title preparation contains a poorly soluble drug and a carrier comprising (a) ≥1 fatty ester of polyglycerol or sorbitan as cosurfactant, (b) ≥1 triglyceride oil, and (c) ≥1 nonionic surfactant with HLB ≥10. Thus, a solution was prepared by heating **cyclosporin** A 100.0, ethoxylated castor oil 400.0, di/tri/tetraglycerol fatty ester 240.0, sesame oil 160.0, and **EtOH** 100.0 mg to 40° and dispensed into soft gelatin **capsules**.

IT **9004-99-3**, Polyoxyethylene monostearate **9005-65-6**, Polyoxyethylene sorbitan monooleate **9005-67-8**, Polysorbate 60 **59865-13-3**, **Cyclosporin** A
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical preparation containing poorly soluble drug with improved bioavailability)

L11 ANSWER 43 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:253420 HCAPLUS
DOCUMENT NUMBER: 120:253420
TITLE: Pharmaceutical compositions containing **cyclosporins**
INVENTOR(S): Richter, Friedrich; Vonderscher, Jacky
PATENT ASSIGNEE(S): Sandoz AG, Switz.
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 589843	A1	19940330	EP 1993-810664	19930921
EP 589843	B1	20011128		
R: BE, CH, DK, ES, GR, IE, IT, LI, LU, NL, PT, SE				
EP 1142568	A1	20011010	EP 2001-109837	19930921
R: BE, CH, DK, ES, GR, IT, LI, LU, NL, SE, PT, IE				
ES 2168271	T3	20020616	ES 1993-810664	19930921

GB 2270842	A1	19940330	GB 1993-19516	19930922
GB 2270842	B2	19970402		
FR 2696094	A1	19940401	FR 1993-11377	19930922
FR 2696094	B1	19950818		
CA 2106827	AA	19940326	CA 1993-2106827	19930923
DE 4332436	A1	19940331	DE 1993-4332436	19930923
AT 9301922	A	20001015	AT 1993-1922	19930923
AT 407703	B	20010525		
JP 06199683	A2	19940719	JP 1993-237805	19930924
JP 2828387	B2	19981125		
US 2002016292	A1	20020207	US 2001-826719	20010405
US 6420355	B2	20020716		
US 2002165134	A1	20021107	US 2002-122756	20020412

PRIORITY APPLN. INFO.:

GB 1992-20245	A	19920925
GB 1992-20246	A	19920925
GB 1992-20247	A	19920925
EP 1993-810664	A3	19930921
US 1993-126946	B1	19930924
US 1995-570273	B1	19951211
US 1997-971432	B1	19971117
US 1998-174904	B1	19981019
US 1999-444974	B1	19991122
US 2001-826719	A1	20010405

AB A pharmaceutical composition in the form of an emulsion preconc. for **oral** administration of **cyclosporin**, contains a carrier medium that contains (1) a hydrophilic organic solvent, (2) a mixed mono-, di-, and tri-glyceride or a transesterified and polyethoxylated vegetable oil, and (3) a polyoxyethylene sorbitan fatty acid ester surfactant. The composition provides high bioavailability and low inter- and intra-subject variability. For example, a **capsule** contained **cyclosporin** 50, 1,2-**propylene glycol** 37, **ethanol** 75, Maisine (glycerol-transesterified corn oil) 113, and **tween** -80 225 mg.

IT **57-55-6**, 1,2-Propanediol, biological studies **64-17-5**, **Ethanol**, biological studies **9005-65-6**, **Tween** 80
RL: BIOL (Biological study)
(**cyclosporin oral** emulsions containing)

IT **59865-13-3**, **Cyclosporin 79217-60-0**, **Cyclosporin**
RL: BIOL (Biological study)
(**oral** emulsions of, transesterified vegetable oils and surfactants in)

L11 ANSWER 44 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER:	1994:38187 HCAPLUS
DOCUMENT NUMBER:	120:38187
TITLE:	Ophthalmic compositions containing **cyclosporins** and surfactants
INVENTOR(S):	Kawashima, Yoichi; Kuwano, Mitsuaki
PATENT ASSIGNEE(S):	Sandoz-Erfindungen Verwaltungsgesellschaft m.b.H., Austria; Sandoz-Patent-G.m.b.H.; Sandoz Pharmaceuticals Ltd.; Sandoz Ltd.
SOURCE:	PCT Int. Appl., 19 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9323010	A1	19931125	WO 1993-EP1123	19930507
W: JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 642332	A1	19950315	EP 1993-909919	19930507
EP 642332	B1	19970115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 07506579	T2	19950720	JP 1993-519842	19930507
AT 147619	E	19970215	AT 1993-909919	19930507
ES 2098739	T3	19970501	ES 1993-909919	19930507
CN 1084079	A	19940323	CN 1993-107203	19930512
CN 1074932	B	20011121		
US 5951971	A	19990914	US 1996-767610	19961217
US 2002045601	A1	20020418	US 2001-939967	20010827
US 6582718	B2	20030624		

PRIORITY APPLN. INFO.:
GB 1992-10226 A 19920513
GB 1992-24367 A 19921120
WO 1993-EP1123 W 19930507
US 2000-641867 A1 20000818

AB An ophthalmic composition contains a **cyclosporin** and a surfactant, e.g, polyoxyethylene fatty acid esters. An **eye -drop** contained **cyclosporin** A 0.05, polyoxyl 40 stearate 2.0, hydroxypropyl Me cellulose 0.3, BTH 0.001, **EtOH** 0.1, NaCl 0.73, NaH2PO4 0.2, NaEDTA 0.1g, NaOH q.s, and water q.s. to 100mL.

IT **9004-99-3**, Polyoxyl 40 stearate
RL: BIOL (Biological study)
(ophthalmic pharmaceuticals containing **cyclosporins** and)

IT **59865-13-3**, **Cyclosporin** a **79217-60-0**, **Cyclosporin**
RL: BIOL (Biological study)
(ophthalmic pharmaceuticals containing surfactants and)

L11 ANSWER 45 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:38157 HCAPLUS
DOCUMENT NUMBER: 120:38157
TITLE: Pharmaceutical composition containing **cyclosporin** derivative
INVENTOR(S): Meinzer, Armin; Richter, Friedrich; Vonderscher, Jacky Francis
PATENT ASSIGNEE(S): Sandox-Erfindungen Verwaltungesellscaft m.b.H., Austria; Sandoz-Patent-G.m.b.H.; Sandoz Ltd.
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9320833	A1	19931028	WO 1993-EP955	19930420

W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, VN
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9342611	A1	19931118	AU 1993-42611	19930420
AU 672793	B2	19961017		
EP 637248	A1	19950208	EP 1993-911768	19930420
EP 637248	B1	20020703		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 07505872	T2	19950629	JP 1993-517998	19930420
HU 71580	A2	19951228	HU 1994-3055	19930420
HU 218279	B	20000728		
RU 2126263	C1	19990220	RU 1994-46413	19930420
CZ 287359	B6	20001115	CZ 1994-2617	19930420
AT 219940	E	20020715	AT 1993-911768	19930420
SK 282745	B6	20021203	SK 1994-1272	19930420
ES 2179052	T3	20030116	ES 1993-911768	19930420
FI 9404978	A	19941021	FI 1994-4978	19941021
NO 9403998	A	19941021	NO 1994-3998	19941021

PRIORITY APPLN. INFO.: GB 1992-8712 A 19920422
WO 1993-EP955 A 19930420

AB **Oral** formulations containing (3'-desoxy-3'-oxo-MeBmt)1-(Val)2-ciclosporin (I) and a carrier medium comprising a hydrophilic phase, a transesterified ethoxylated vegetable oil, and a surfactant are prepared A **capsule** contained I 100, absolute **EtOH** 105, Labrafil M2125 150, 1,2-**propylene glycol** 95, Cremophor RH40, and α-tocopherol 1mg. There was no change in the appearance of the content of the **capsules** after storage at 30° and 65% humidity for 12 mo. The **capsules** had higher bioavailability than com. soft-gelatin **capsules** of **cyclosporin** in dogs.

IT **57-55-6**, 1,2-Propanediol, biological studies **64-17-5**, **Ethanol**, biological studies **9005-65-6**, **Tween** 80
RL: BIOL (Biological study)
(**oral** pharmaceuticals containing **cyclosporin** derivative and)

L11 ANSWER 46 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:456164 HCAPLUS
DOCUMENT NUMBER: 119:56164
TITLE: **Oral** compositions of proteinaceous medicaments
INVENTOR(S): Desai, Ashok J.
PATENT ASSIGNEE(S): Applied Analytical Industries, Inc., USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5206219	A	19930427	US 1991-797221	19911125

PRIORITY APPLN. INFO.: US 1991-797221 19911125

AB Proteinaceous medicaments (e.g. erythropoietin, insulin, calcitonin)

are formulated in a medium containing a polyol pharmaceutical solvent combined as cosolvent with a lipid pharmaceutical solvent. The formulation is adapted for **oral** administration as a liquid as well as a filled hard or soft gelatin **capsule**. The preferred polyol solvent is PEG/**propylene glycol**, and the preferred lipid solvent is oleic acid. A **capsule** formulation contained (per **capsule**) insulin 140 IU, dimyristyl phosphatidylcholine 0.047, aprotinin 3.39, hydroxypropyl cellulose-LF 3.76, poly-oxy 40 stearate 3.76, PEG 400 139.8, **propylene glycol** 15.57, water/citrate buffer (pH adjustment) 8.75, cholesterol 31.2, **Tween**-80 17.56, egg yolk lecithin 63.1, glyceryl monooleate 27.9, d-α-tocopherol 19.6, and oleic acid 249.1 mg.

IT **57-55-6, Propylene glycol**, biological studies
RL: BIOL (Biological study)
(enteric pharmaceutical of protein with)

IT **59865-13-3, Cyclosporin**
RL: BIOL (Biological study)
(enteric pharmaceutical of, polyol and lipid in)

IT **9005-65-6, Tween** 80
RL: BIOL (Biological study)
(in insulin **capsule** formulation with PEG and lipid)

L11 ANSWER 47 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:221601 HCAPLUS
DOCUMENT NUMBER: 116:221601
TITLE: Preparation of bioadhesive **capsules** containing cyclic peptide immunosuppressants
INVENTOR(S): Huettenrauch, Reinhard
PATENT ASSIGNEE(S): Jenapharm G.m.b.H., Germany
SOURCE: Ger. (East), 3 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 298351	A5	19920220	DD 1989-334244	19891106

PRIORITY APPLN. INFO.: DD 1989-334244 19891106

AB The title active agent is dissolved in a C3-5 polyhydric alc, transferred to a melt of ≤3 carrier substances, solidification is induced with a saturated organic acid Me(CH2)nCO2H (n = 12-20), and the mass is enclosed in a gelatin **capsule**. Thus, 200 g **cyclosporin** was dissolved in 200 g 1,2-**propylene glycol** at 70°, 100 g polysorbate and 150 g stearic acid were added at the same temperature to provide a melt, and 325 g of the melt was loaded into gelatin **capsules**.

IT **59865-13-3, Cyclosporin 59865-13-3D, Cyclosporin**, derivs.
RL: BIOL (Biological study)
(bioadhesive **capsules** containing)

IT **57-55-6**, 1,2-**Propylene glycol**, biological studies **9005-67-8**
RL: BIOL (Biological study)

(bioadhesive **capsules** containing cyclic peptides and melt containing)

L11 ANSWER 48 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:136281 HCAPLUS
DOCUMENT NUMBER: 116:136281
TITLE: Formulation of hydrophobic and/or lipophilic peptide drugs
INVENTOR(S): Dauth, Christoph; Decker, Karl Ludwig; Geissler, Sabine; Heidenbluth, Karlheinz; Hempel, Roland; Hoffmann, Evelyn; Poetter, Heinrich; Rattke, Wilfried; Rudat, Wolf Ruediger; et al.
PATENT ASSIGNEE(S): Arzneimittelwerk Dresden G.m.b.H., Germany
SOURCE: Ger. (East), 4 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 295765	A5	19911114	DD 1988-318014	19880718

PRIORITY APPLN. INFO.: DD 1988-318014 19880718

AB Solns. of hydrophobic and/or lipophilic peptide drugs, such as **cyclosporins**, are blended into water or aqueous solns. of surfactants, low mol.-weight carbohydrates, salts, etc. The precipitate obtained, optionally lyophilized, is incorporated into a hydrophilic polymer matrix. A solution of 100g **cyclosporin** A in 1 L **EtOH** was blended into 5 L aqueous 0.5% NH4AcO solution, to give a precipitate which was lyophilized and homogenized, at 45°, with 250 mL of an aqueous solution of 1% agar, and 0.5% **Tween** 40. Cooling of the mixture gave a gel, which was homogenized and filled into gelatin **capsules**.

IT **59865-13-3**, **Cyclosporin** A
RL: PROC (Process)
(formulation of)

IT **9004-99-3**, **Myrj** **9005-66-7**, **Tween** 40
RL: BIOL (Biological study)
(in formulation of peptide drugs)

L11 ANSWER 49 OF 49 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1980:537937 HCAPLUS
DOCUMENT NUMBER: 93:137937
TITLE: **Cyclosporin** A prolongation of segmental pancreatic and islet allograft function in rats
AUTHOR(S): Rynasiewicz, J. J.; Sutherland, D. E. R.; Kawahara, K.; Gorecki, P.; Najarian, J. S.
CORPORATE SOURCE: Health Sci. Cent., Univ. Minnesota, Minneapolis, MN, USA
SOURCE: Transplantation Proceedings (1980), 12(2), 270-4
CODEN: TRPPA8; ISSN: 0041-1345
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A formulation of **cyclosporin** A (I) [**59865-13-3**] in an Intralipid-**EtOH** vehicle provided effective

immunosuppression. A min. dose of I that completely prevented rejection when dissolved in this vehicle and administered i.p. was 1/2 the effective gavage dose of I formulated in **Tween** 80-**EtOH**. Rats receiving I i.p. appeared much healthier than those receiving gavage. The peritoneal cavity of i.p. **injected** rats at interval laparotomy or autopsy showed no evidence of drug precipitation or adhesion formation. I administered **i.v.** (Intralipid-**EtOH**) for the 1st 4 posttransplant days followed by gavage administration resulted in only 1 allograft rejection over the period of observation. I thus may provide more adequate immunosuppression and eliminate the need for diabetogenic agents.

IT **59865-13-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(in Intralipid-**ethanol** vehicle, immunosuppressive activity of)

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:53:29 ON 22 OCT 2003)
L12 23 S L11
L13 21 DUP REM L12 (2 DUPLICATES REMOVED)

L13 ANSWER 1 OF 21 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-636566 [60] WPIDS
DOC. NO. CPI: C2003-173957
TITLE: Formulation useful for increasing bioavailability of orally administered hydrophilic macromolecule, comprising hydrophilic macromolecule, permeation enhancer, and carrier capable of forming bioadhesive gel.
DERWENT CLASS: A96 B04 B05 B07
INVENTOR(S): CHAO, A C; DADDONA, P E; DONG, L C; NGUYEN, V A; WONG, P S L; YUM, S
PATENT ASSIGNEE(S): (ALZA) ALZA CORP
COUNTRY COUNT: 99
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003053401	A2	20030703	(200360)*	EN	40

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003053401	A2	WO 2002-US41031	20021218

PRIORITY APPLN. INFO: US 2001-343005P 20011219
AN 2003-636566 [60] WPIDS

AB WO2003053401 A UPAB: 20030919
NOVELTY - A formulation (F1) comprises a hydrophilic macromolecule, a permeation enhancer, and a carrier capable of forming a bioadhesive gel. (F1) is released within the gastrointestinal tract as a liquid and forms a bioadhesive gel in-situ after the formulation has some opportunity to spread across the surface of the gastrointestinal mucosal membrane.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a dosage form comprising (F1) and a delivery device configured to release (F1) in the gastrointestinal tract; and

(2) a controlled release dosage form comprising a liquid formulation containing a hydrophilic macromolecule and the delivery device.

USE - For increasing the bioavailability of an orally administered hydrophilic macromolecule comprising polypeptide (e.g. insulin, human growth hormone, IFN- alpha , salmon calcitonin, erythropoietin (EPO), TPA (activase), G-CSF (Neupogen), Factor VIII (kogenate), growth hormone-releasing peptide, beta -casomorphine, renin inhibitor, tetragastrin, pepstatinylglycine, leuprolide, empedopeptin, beta -lactoglobulin, TRH analog, ACE inhibitor or **cyclosporine**), polysaccharide (e.g. pentosan polysulfate sodium (PPS), unfractionated heparin, and low molecular weight heparin (LMWH)) (claimed).

ADVANTAGE - The formulation more reliably enhances the **oral** bioavailability of the hydrophilic macromolecules.
Dwg.0/41

L13 ANSWER 2 OF 21 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-645855 [61] WPIDS
DOC. NO. CPI: C2003-176571
TITLE: Composition useful for increasing **oral** bioavailability of poorly soluble drug comprises an oil/water/oil double microemulsion incorporated into a solid support.
DERWENT CLASS: A96 B07
INVENTOR(S): CARLI, F; CHIELLINI, E
PATENT ASSIGNEE(S): (REME-N) REMEDIA SRL
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003051334	A2	20030626	(200361)*	EN	20

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003051334	A2	WO 2002-EP14472	20021218

PRIORITY APPLN. INFO: IT 2001-MI2694 20011219
AN 2003-645855 [61] WPIDS
AB WO2003051334 A UPAB: 20030923
NOVELTY - A pharmaceutical composition containing a poorly soluble drug in powder or microgranular form, comprises an oil/water/oil double microemulsion incorporated into a solid support formed by a microporous inorganic substance, an adsorbent colloidal inorganic substance or by a cross-linked swellable in water polymer. The drug is dissolved or dispersed in at least one phase of the microemulsion.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for preparation of the composition involving:

(a) dissolution of the drug in an oil or in a mixture of oils;

(b) addition of the oil solution of step (A) to water or to an aqueous solution;

(c) addition of a surfactant and optionally of a co-surfactants to the mixture of step (B) and agitation with the formation of an oil/water microemulsion;

(d) addition of oil/water microemulsion of stage (C) to an oil or to a mixture of oils optionally containing drug, surfactant and/or cosurfactant and agitation with formation of the oil/water/oil microemulsion; and

(e) incorporation of the oil/water/oil microemulsion of stage (D) into a support in the form of a powder.

USE - For increasing **oral** bioavailability of poorly soluble drug (e.g. megestrol acetate, hydrocortisone acetate, ubidecarenone, lovastatin, **cyclosporin**, pyroxican, nifedipine, isoflavone, temazepam, carbamazepine, glibenclamide, progesterone and ibuprofen) (claimed).

ADVANTAGE - The composition improves the solubility and the velocity of dissolution of the drug. The sizes of the oil microdrops released by the solid support in an aqueous environment are about less than 1 micrometer. The velocity of dissolution determined in aqueous buffer at physiological pH is superior to that attainable with oil/surfactant mixtures or with simple microemulsions. The solubility kinetics determined in aqueous buffer at physiological pH is superior to the kinetics attainable with oil/surfactant mixtures or with simple microemulsions.

Dwg.0/10

L13 ANSWER 3 OF 21 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-430331 [40] WPIDS
CROSS REFERENCE: 2003-441191 [41]; 2003-457255 [43]
DOC. NO. CPI: C2003-113759
TITLE: Composition useful for producing immunosuppression comprises an isomeric mixture of a **cyclosporine** analog modified at the 1-amino acid residue with a 1,3-diene substituent.
DERWENT CLASS: B04
INVENTOR(S): FOSTER, R T; NAICKER, S; YATSCOFF, R W
PATENT ASSIGNEE(S): (ISOT-N) ISOTECHNIKA INC
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003033527	A2	20030424	(200340)*	EN	41

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE
LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ
DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP
KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ
NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ
UA UG US UZ VC VN YU ZA ZM ZW
US 2003139326 A1 20030724 (200352)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003033527 A2		WO 2002-CA1560	20021017
US 2003139326 A1	Provisional	US 2001-346201P	20011019
	Provisional	US 2002-370596P	20020405
		US 2002-274255	20021017

PRIORITY APPLN. INFO: US 2001-346201P 20011019; US 2002-370596P 20020405; US 2002-274255 20021017

AN 2003-430331 [40] WPIDS

CR 2003-441191 [41]; 2003-457255 [43]

AB WO2003033527 A UPAB: 20030813

NOVELTY - A composition comprises an isomeric mixture of a **cyclosporine** analog modified at the 1-amino acid residue with a 1,3-diene substituent. The isomeric mixture comprises for the diene substituent 10 - 90% of E- and 10 - 90% of Z-isomer.

ACTIVITY - Immunosuppressive; Antiinflammatory; Antiarthritic; Antirheumatic; Antianemic; Hemostatic; Dermatological; Hepatotropic; Virucide; Gastrointestinal; Antiulcer; Ophthalmological; Antithyroid; Neuroprotective; Antidiabetic; Antipsoriatic; Nephrotropic; Endocrine; Antiallergic; Antiasthmatic; Thrombolytic; Cytostatic.

The efficacy of an isomeric mixture of **cyclosporine** analog (45 - 50% of E-isomer and 50 - 55% of Z-isomer) (A) in preventing the rejection of hearts transplanted between different stains of Wistar Furth rats to Lewis rats was assessed and compared to that of **cyclosporine** A (control). Intraperitoneal **injection** of either **cyclosporine** A or (A) were given to the transplant recipient starting 3 days prior to transplantation and continuing for 30 days post-transplantation. The average survival rates of (A)/control at a dose of 1.75 mg/kg/day was 57 plus or minus 32/18 plus or minus 7. The results showed that (A) at an optimal dose of 1.75 mg/kg/day increased survival time approximately 3-fold over **cyclosporine** A.

MECHANISM OF ACTION - None given.

USE - For producing immunosuppression in animal (preferably human); for reducing the toxicity of an immunosuppressive **cyclosporine** analog; for increasing the efficacy of an immunosuppressive **cyclosporine** analog; for treating or alleviating acute organ or tissue transplant rejection (e.g. heart, lung, combined heart-lung, liver, kidney, pancreatic, skin, bowel or corneal), T-cell mediated rejection, graft-versus-host disease (e.g. following bone marrow transplantation), chronic rejection (e.g. graft vessel disease) of a transplanted organ, xenograft rejection (e.g. acute, hyperacute and chronic rejection of an organ occurring when the organ donor is of a different species from the recipient or

a rejection mediated by B-cells or antibody-mediated rejection), autoimmune disease or condition or an inflammatory disease or condition (e.g. arthritis, rheumatoid arthritis, arthritis chronica progrediente, arthritis deformans, other rheumatic diseases, hematological disorders, hemolytic anemia, aplastic anemia, pure red cell anemia, idiopathic thrombocytopenia, systemic lupus erythematosus, polychondritis, scleroderma, Wegener granulomatosis, dermatomyositis, chronic active hepatitis, myasthenia gravis, psoriasis, Steven-Johnson syndrome, idiopathic sprue, (autoimmune) inflammatory bowel disease, ulcerative colitis, Crohn's disease, endocrine ophthalmopathy, Graves disease, sarcoidosis, multiple sclerosis, primary biliary cirrhosis, juvenile diabetes (diabetes mellitus type I), uveitis (anterior and posterior), keratoconjunctivitis sicca, vernal keratoconjunctivitis, interstitial lung fibrosis, psoriatic arthritis, glomerulonephritis, idiopathic nephrotic syndrome, minimal change nephropathy, juvenile dermatomyositis, psoriasis, contact dermatitis, atopic dermatitis, alopecia areata, erythema multiforma, dermatitis herpetiformis, scleroderma, vitiligo, hypersensitivity angiitis, urticaria, bullous pemphigoid, lupus erythematosus, pemphigus, epidermolysis bullosa acquisita, other inflammatory or allergic conditions of the skin, inflammatory conditions of the lungs and airways, asthma, allergies or pneumoconiosis) (all claimed).

ADVANTAGE - The mixtures possess enhanced efficacy and reduced toxicity over the individual isomers and over naturally occurring and other presently known cyclosporines and **cyclosporine** derivatives. The **cyclosporine** analog has a potent immunosuppressant activity.

Dwg.0/13

L13 ANSWER 4 OF 21 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-457255 [43] WPIDS
CROSS REFERENCE: 2003-430331 [40]; 2003-441191 [41]
DOC. NO. CPI: C2003-121635
TITLE: Micro emulsion pre concentrates and formulations containing **cyclosporin** analogs, useful for treating inflammatory or autoimmune diseases or conditions.
DERWENT CLASS: A96 B02 B03 B07
INVENTOR(S): FOSTER, R T; NAICKER, S A; YATSCOFF, R W; NAICKER, S
PATENT ASSIGNEE(S): (ISOT-N) ISOTECHNIKA INC; (YATS-I) YATSCOFF R W
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003032949	A1	20030424	(200343)*	EN	44
US 2003171264	A1	20030911	(200367)		

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003032949 A1		WO 2002-CA1561	20021017
US 2003171264 A1	Provisional	US 2001-346201P	20011019
	Provisional	US 2002-370597P	20020405
		US 2002-274419	20021017

PRIORITY APPLN. INFO: US 2002-370597P 20020405; US 2001-346201P 20011019; US 2002-274419 20021017

AN 2003-457255 [43] WPIDS

CR 2003-430331 [40]; 2003-441191 [41]

AB WO2003032949 A UPAB: 20031017

NOVELTY - Micro emulsion pre concentrates and formulations contain **cyclosporin** analogs.

DETAILED DESCRIPTION - A Micro emulsion pre concentrate or formulation comprises:

(a) **cyclosporin** analog ISATx247;

(b) vitamin E TPGS;

(c) medium chain triglyceride (MCT) oil;

(d) an emulsifier selected from **Tween** 40 and **Tween** 80; and

(e) **ethanol**.

INDEPENDENT CLAIMS are also included for:

(1) formulations comprising (i) ISATx247; MCT oil; **Tween** 80; triacetin and **ethanol**; or (ii) ISATx247; **Tween** 80; vitamin E TPGS; **ethanol**; and isopropyl myristate;

(2) preparation of the pre concentrates and formulations; and

(3) use of the pre concentrates and formulations for producing immunosuppression; or increasing the immunosuppressive effects of ISATx247.

ACTIVITY - Immunosuppressive; Antiinflammatory; Thyromimetic; Antianemic; Antipsoriatic; Antidiabetic; Antirheumatic; Antiarthritic; Dermatological; Neuroprotective; Uropathic; Ophthalmological; Hepatotropic; Virucide; Nephrotropic; Protozoacide.

MECHANISM OF ACTION - None given in the source material.

USE - The formulations are useful for producing immunosuppression; or increasing the immunosuppressive effects of ISATx247, and treating inflammatory or autoimmune diseases or conditions (claimed). They can be used to prevent organ rejection or graft versus host disease, and to treat e.g. Hashimoto's thyroiditis, pernicious anemia, Addison's disease, psoriasis, diabetes, rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis, Sjoegren's syndrome, lupus erythematosus, multiple sclerosis, myasthenia gravis, Reiter's syndrome, arthritis, rheumatic disease, autoimmune hematological disorder, polychondritis, scleroderma, Wegener granulamatosis, dermatomyositis, chronic active hepatitis, Steven-Johnson syndrome, autoimmune inflammatory bowel disease, endocrine ophthalmopathy, Grave's disease, sarcoidosis, primary biliary cirrhosis, uveitis, keratoconjunctivitis sic ca, vernal keratoconjunctivitis, interstitial lung fibrosis, psoriatic arthritis or glomerulonephritis.

The formulations may also be used to treat anti-parasitic or anti-protozoal disease, e.g. malaria, cocidiodomycosis or

schistosomasis; or to reverse or abrogate anti-neoplastic agent resistance in tumors.

ADVANTAGE - The Micro emulsions are stable and provide high drug solubility, superior drug bioavailability and may reduce adverse effects associated with administration of **cyclosporin**.

In pharmacokinetic studies carried out in dogs, a formulation (A) comprising ISATx247 and VitE-TPGS/MCT oil/**Tween** 40/ **ethanol** (4/2/2/1 by weight), and Neoral were administered by **oral** gavage (2 ml, 100 mg/ml). Blood levels of ISATx247 were monitored at intervals up to 24 hours post dosing. Results for (A) and Neoral respectively were: Cmax (ng/ml) 1439 plus or minus 378 and 2158 plus or minus 677; and AUC 8290 and 11460. The bioavailability from (A) was comparable to that of Neoral, and was substantially greater than the bioavailability provided by Sandimmune (data not given).

Dwg.0/5

L13 ANSWER 5 OF 21 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2003-201234 [19] WPIDS
DOC. NO. CPI: C2003-051081
TITLE: Topical scalp and transdermal preparation useful for treating diseases related to hair loss comprises a carrier **encapsulated** **cyclosporin** derivative.
DERWENT CLASS: A96 B04 D21 E12
INVENTOR(S): KIM, J C; AHN, H; CHO, H; KIM, H; KIM, J; KIM, S; LEE, C; LEE, H; LEE, M; PARK, S
PATENT ASSIGNEE(S): (GLDS) LG HOUSEHOLD & HEALTH CARE LTD
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002092031	A1	20021121	(200319)*	EN	17
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW					
KR 2002087647	A	20021123	(200320)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002092031	A1	WO 2002-KR861	20020509
KR 2002087647	A	KR 2001-26503	20010515

PRIORITY APPLN. INFO: KR 2001-26503 20010515

AN 2003-201234 [19] WPIDS

AB WO 200292031 A UPAB: 20030320

NOVELTY - A topical scalp and transdermal preparation for promoting hair growth, comprises a carrier **encapsulated** **cyclosporin** derivative (A). The carrier is liposome,

microcapsule, microsphere, composite particle or emulsion.

DETAILED DESCRIPTION - A topical scalp and transdermal preparation comprises a carrier **encapsulated** **cyclosporin** derivative (A). The carrier is liposome, microcapsule, microsphere, composite particle or emulsion. (A) is (gamma -hydroxy-N-methyl-L-leucine4) derivative of formula (I).

A = N-methyl-(4R)-4-((E)-2-butenyl)-4-methyl-L-threonine, (2S,3R,4R,6E)-3-sulfhydryl-4-methyl-2-(methylamino)-6-octenoic acid or (2S,4R,6E)-3-oxo-4-methyl-2-(methylamino)-6-octenoic acid;

B = L- alpha -aminobutyric acid (Abu), L-alanine (Ala), L-threonine (Thr), L-valine (Val) or L-norvaline (Nva);

C1 = CH3NH-CH(R)-COOH or -X-R';

R, R' = 1-6C alkyl, alkenyl or alkynyl (all optionally substituted by at least one of amino, hydroxy, (halo)alkyl, ester, alkoxy, cyano, nitro or (di)alkylamino) or H;

X = O or S;

HMeLeu = gamma -hydroxy-N-methyl-L-leucine;

D = L-valine, L-norvaline or L-leucine;

E, H, I = N-methyl-L-leucine, HmeLeu or L-leucine;

F1 = L-alanine or L-alanine thioamide ((7 psi 8 CS-NH), NH-CHCH3-CS);

G = D-hydroxyisovaleric acid or NH-CH(CH2-R1)-COOH;

R1 = H or XR'; and

J = N-methyl-L-valine or L-valine.

INDEPENDENT CLAIMS are included for the following:

(1) Preparation of liposome involving either dissolving amphiphilic molecules and **cyclosporin** derivative in an organic solvent (a), evaporating (a) at ambient temperature giving a mixture of dry lipid film comprising amphiphilic molecules and (A), hydrating the dry film by adding an aqueous solution and homogenizing the resultant film using a mechanical dispersion instrument, or dissolving (A) in an oil phase, emulsifying the oil phase in an aqueous solution and creating a chemical reaction of **capsule** wall materials in the aqueous phase of the emulsion;

(2) Preparation of a microcapsule involving dissolving (A) and a polymer in an oil phase, dispersing the oil phase in a second immiscible phase and evaporating the oil phase;

(3) Preparation of a composite particle involving mixing (A) and surfactant in an aqueous phase and forcibly dispersing the solution using a mechanical dispersion instrument; and

(4) Preparation of emulsion involving emulsifying (A) in an oil phase or an aqueous phase containing an emulsifying agent.

ACTIVITY - Dermatological.

MECHANISM OF ACTION - Hair growth stimulator.

USE - The composition is used for promoting hair growth (claimed), and for treating hair-loss e.g. human male alopecia. It is also useful for manufacturing composition for use on hairs, such as shampoos or rinses.

ADVANTAGE - The formulation can penetrate the skin and follicle and has an excellent in-vivo hair restoring effect without immunosuppressive activity. The carriers used have an excellent drug delivery effect. The carrier particles show good dispersion and phase stability over time in compositions for use in hair.

A test liposome formulation comprised a **cyclosporin** derivative (gamma -hydroxy-N-methyl-L-leucine4)**cyclosporin** A and phosphatidylcholine (10 weight%). A comparative liposome formulation comprised (gamma -hydroxy-N-methyl-L-leucine4) **cyclosporin** A (5%) in acetone. An in vitro test was

performed to evaluate skin penetration ability of test and control liposome formulations. Skin of 6-8 week old, female hairless SKH1 mice was positioned between a diffusion cell comprising a donor chamber and a receptor chamber. The epidermis was directed to the donor chamber and dermis was directed to the receptor chamber. Phosphate-buffered saline (pH 7.4, 37 deg. C) was added to the receptor chamber and was allowed to stand for 1 hour. The test liposome suspension (300 mg, 5% **cyclosporin**) and control suspension was respectively applied to the dermis. The donor chamber was sealed with paraffin. After 12 hours, a 0.2 ml fluid was sampled from the receptor chamber and the amount of the **cyclosporin** derivative penetrated through skin was determined and found to be 3.78/0.97 (for test/control formulation). It was observed that the fine particles of several microns in size showed 2-3 times higher skin penetration than those of free **cyclosporin** derivatives dissolved in acetone. Thus, the test formulation had an advantage of higher skin penetration than that of comparative **cyclosporin** formulation at a molecular level.
Dwg.0/0

L13 ANSWER 6 OF 21 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-018611 [01] WPIDS
DOC. NO. CPI: C2003-004399
TITLE: Liquid compositions useful in drug delivery systems comprises monoglyceride compound, emulsifier, aqueous solution, organic solvent and optionally bioactive compound.
DERWENT CLASS: A96 B05 B07
INVENTOR(S): JUNG, H S; JUNG, S Y; KWON, I C; CHUNG, H; JEONG, S; KWON, I
PATENT ASSIGNEE(S): (KOAD) KOREA ADV INST SCI & TECHNOLOGY
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002064166	A1	20020822	(200301)*	EN	42

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

KR 2002066778 A 20020821 (200310)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002064166	A1	WO 2002-KR206	20020208
KR 2002066778	A	KR 2001-7125	20010213

PRIORITY APPLN. INFO: KR 2001-7125 20010213
AN 2003-018611 [01] WPIDS
AB WO 200264166 A UPAB: 20030101
NOVELTY - A liquid composition (A) comprises (weight%) at least one

monoglyceride compound (a) (9 -90) as an uptake enhancer, at least one emulsifier (b) (0.01 - 80), aqueous solution (c) (0.01 - 10) and at least one organic solvent (d) (0.001 - 90) to solubilize the bioactive compound.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) A powder composition (B) for enhanced bioavailability of bioactive compound (e) manufactured by lyophilization of the dispersion of (A) by adding a cryoprotectant (m) (0 - 30 weight%);

(2) Preparation of (A) comprising:

(a) preparing a viscous liquid by dissolving (a) and (b) in (d) containing (c); and

(b) removing the volatile (d); and

(3) Preparation of (B) comprising:

(a) dispersing (A) in water to prepare the dispersion; and

(b) lyophilizing the resulting product in the presence of (m).

USE - In drug delivery systems.

ADVANTAGE - The formulation enhances bioavailability of bioactive materials and has high **encapsulation** efficiency of the bioactive material. It has long-term storage because it does not contact with an organic solvent or moisture and can solubilize and **encapsulate** bioactive compounds with a low bioavailability such as peptides or proteins stably and also generate homogenous particles less than 500 nm when dispersed in water. It can be easily dispersed in water without any mechanical aid, and problems such as phase separation, hydrolysis, and oxidation, during long-term storage do not occur.

Dwg.0/0

L13 ANSWER 7 OF 21 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2002-454375 [48] WPIDS

DOC. NO. CPI: C2002-129117

TITLE: A selfemulsifiable formulation, useful in immunosuppression therapy, comprises an immunosuppression agent, hydrophilic agent, lipophilic agent, one or more surfactants, antioxidant and preservatives.

DERWENT CLASS: A96 B03

INVENTOR(S): BHARTI, P; CHAKRAVORTY, S

PATENT ASSIGNEE(S): (RPGL-N) RPG LIFE SCI LTD

COUNTRY COUNT: 95

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002022158	A1	20020321	(200248)*	EN	42
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
BR 2000013813	A	20020430	(200246)		
AU 2001025459	A	20020326	(200251)		
EP 1333851	A1	20030813	(200355)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002022158	A1	WO 2000-IN91	20000918
BR 2000013813	A	BR 2000-13813	20000918
		WO 2000-IN91	20000918
AU 2001025459	A	WO 2000-IN91	20000918
		AU 2001-25459	20000918
EP 1333851	A1	EP 2000-988993	20000918
		WO 2000-IN91	20000918

FILING DETAILS:

PATENT NO	KIND		PATENT NO
BR 2000013813	A	Based on	WO 2002022158
AU 2001025459	A	Based on	WO 2002022158
EP 1333851	A1	Based on	WO 2002022158

PRIORITY APPLN. INFO: WO 2000-IN91 20000918
AN 2002-454375 [48] WPIDS
AB WO 200222158 A UPAB: 20020730
NOVELTY - A selfemulsifiable formulation for **oral** administration comprises an immunosuppression agent, hydrophilic agent, lipophilic agent, one or more surfactants, antioxidant and preservatives.

DETAILED DESCRIPTION - A selfemulsifiable formulation for **oral** administration comprises an immunosuppression agent, hydrophilic agent, lipophilic agent, one or more surfactants, antioxidant and preservatives. The immunosuppression agent is preferably lactam macrolide. The hydrophilic agent is selected from 1-4C lower alkanols, alkylene glycol monoalkyl ethers, low molecular weight monooxy-alkane-diol, low molecular weight polyoxy-alkane-diol, 1,2-propyleneglycol, particularly **ethanol**. The lipophilic agent is selected from saturated polyglycolyzed 8-10C glycerides, particularly transesterified caprylic and capric glycerides, polyoxyethylene sorbitan fatty acid esters, particularly polysorbate 80, **polyoxyethylene castor oil** derivatives, particularly cremophor RH 40. The antioxidant is selected from alpha-tocopherol, ascorbyl palmitate, butyl hydroxy anisole, butyl hydroxy toluene, propyl gallate. The preservative is selected from **ethanol**, benzyl alcohol.

An INDEPENDENT CLAIM is also included for a method of preparing the selfemulsifiable formulation.

ACTIVITY - Immunosuppressive.

MECHANISM OF ACTION - None given in the source material.

USE - This formulation is used in immunosuppression therapy.

ADVANTAGE - This formulation has enhanced bioavailability, bio-absorption, increased solubility, transport rate, has improved capability to release the drug in a reduced time with reduced toxicity. Also, it can be stored in the tropical countries for a longer period of time.

Dwg.0/6

L13 ANSWER 8 OF 21 EMBASE

RESERVED. on STN
ACCESSION NUMBER: 2002407042 EMBASE
TITLE: Improved **oral** bioavailability of **cyclosporin** A in male Wistar rats: Comparison of a Solutol HS 15 containing self-dispersing formulation and a microsuspension.
AUTHOR: Bravo Gonzalez R.C.; Huwyler J.; Walter I.; Mountfield R.; Bittner B.
CORPORATE SOURCE: B. Bittner, Pharmaceuticals Division, Discovery DMPK, F. Hoffmann-La Roche Ltd., Grenzacher Strasse 124, CH-4070 Basel, Switzerland. beate.bittner@roche.com
SOURCE: International Journal of Pharmaceutics, (1 Oct 2002) 245/1-2 (143-151).
Refs: 30
ISSN: 0378-5173 CODEN: IJPHDE
PUBLISHER IDENT.: S 0378-5173(02)00339-3
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Oral** bioavailability of the highly lipophilic and poorly water-soluble immunosuppressive agent **cyclosporin** A (CyA) in two different formulations was investigated in male Wistar rats. An aqueous microsuspension and a self-dispersing formulation composed of the surface-active ingredients Solutol HS 15:Labrafil M2125CS:oleic acid=7:2:1 (v/v/v) were administered to the animals at a dose level of 20 mg/kg. In order to calculate the absolute **oral** bioavailability, CyA was additionally administered **intravenously** at 10 mg/kg as microsuspension. It was found that the **oral** bioavailability of CyA in the Solutol HS 15-based formulation was twofold higher as compared to the microsuspension (69.9±2.8 vs. 35.7±3.3%, P=0.001). By contrast, the time to reach maximum plasma concentration (t(max)) and the terminal half-life (t(1/2)) did not differ significantly with the different formulations (t(max): 7.0±1.0 vs. 6.3±1.7 h; t(1/2): 20.5±2.9 vs. 16.7±4.7 h). In vitro solubility experiments demonstrated a marked increase in the aqueous solubility of CyA in the presence of the self-dispersing formulation as compared to the micronized powder alone (solubility after 120 min at 37°C: 136 vs. 23.2 μg/ml in human gastric juice; 133 vs. 10.8 μg/ml in simulated intestinal juice). Most likely, the enhanced systemic exposure of CyA in the self-dispersing formulation was caused by improved solubility of CyA in the gastrointestinal fluids in the presence of the surface-active ingredients. Additional factors that may have contributed to increased **oral** bioavailability are inhibition of metabolism and/or transport processes as well as permeability enhancement by the co-administered excipients. .COPYRGT. 2002 Elsevier Science B.V. All rights reserved.

L13 ANSWER 9 OF 21 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-010545 [01] WPIDS
DOC. NO. CPI: C2002-002528
TITLE: Solubilizing composition for use in medical/pharmaceutical fields such as drug delivery

system, comprises preset amount of mono-glyceride compound, emulsifier, water-insoluble material, organic solvent and additives.

DERWENT CLASS: A96 A97 B07 E19 J04

INVENTOR(S): JUNG, H S; JUNG, S Y; KWON, I C; CHUNG, H; JEONG, S Y

PATENT ASSIGNEE(S): (KOAD) KOREA ADV INST SCI & TECHNOLOGY; (CHUN-I) CHUNG H; (JEON-I) JEONG S Y; (KWON-I) KWON I C

COUNTRY COUNT: 95

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001068139	A1	20010920	(200201)*	EN	47
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001041245	A	20010924	(200208)		
KR 2001100194	A	20011114	(200230)		
EP 1263468	A1	20021211	(200301)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
US 2003099675	A1	20030529	(200337)		
CN 1422163	A	20030604	(200356)		
JP 2003526679	W	20030909	(200360)		39

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001068139	A1	WO 2001-KR389	20010313
AU 2001041245	A	AU 2001-41245	20010313
KR 2001100194	A	KR 2000-12465	20000313
EP 1263468	A1	EP 2001-912555	20010313
		WO 2001-KR389	20010313
US 2003099675	A1	WO 2001-KR389	20010313
		US 2002-221449	20020912
CN 1422163	A	CN 2001-807593	20010313
JP 2003526679	W	JP 2001-566702	20010313
		WO 2001-KR389	20010313

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001041245	A	Based on	WO 2001068139
EP 1263468	A1	Based on	WO 2001068139
JP 2003526679	W	Based on	WO 2001068139

PRIORITY APPLN. INFO: KR 2000-12465 20000313

AN 2002-010545 [01] WPIDS

AB WO 200168139 A UPAB: 20020105

NOVELTY - A solubilizing composition (SLC) comprises (in weight% (weight%)) mono-glyceride compound(s) (9-90), emulsifier(s) (0.01-90),

water-insoluble material(s) (0-50), organic solvent (OS) (0-90.9), and additives (0-5).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (i) Preparation of the SLC which involves dissolving mono-glyceride compound(s), emulsifier(s) and water-insoluble material(s), in OS, and removing OS; (ii) A liquid formulation which comprises (in weight%) SLC (1-99) and OS (1-99); (iii) Preparation of homogeneous liquid formulation which involves mixing SLC with OS; (**iv**) A powder formulation which is prepared by lyophilizing the liquid formulation dispersion, by adding with 0-30 weight/volume% (w/v%) of cryoprotectant; (v) Preparation of the powder formulation which involves dispersing the liquid formulation in excess water, and lyophilizing the dispersed liquid by adding cryoprotectant; (vi) A water-insoluble solubilizing liquid formulation which comprises (in weight%) mono-glyceride compound(s) (9-90), emulsifier(s) (0.01-90), pharmaceutical compound(s) (0.001-50), OS (9-90) and additives (0-5); (vii) Preparation of solubilizing liquid formulation which involves dissolving mono-glyceride compound(s), pharmaceutical compound(s) and emulsifier(s), in OS, and removing OS, to obtain a composition which is mixed with OS; (viii) A solubilizing powder formulation which is prepared by lyophilizing the solubilizing liquid formulation dispersion, by adding with 0-10 w/v% of cryoprotectant; and (ix) Preparation of the solubilizing powder formulation, as above powder formulation.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - For use in medical/pharmaceutical fields such as drug delivery system.

ADVANTAGE - The solubilizing composition enables stable solubilization of materials such as pharmaceutical compounds, and also stable long-term storage. The homogeneous liquid formulation can be easily dispersed in water, without using any harsh physical force, to form dispersion of particles of less than 500 nm. The liquid formulation is physically stable as it is a single phase liquid, and also chemically stable as it does not contain water and does not require any physical force during the formulation process. Cryoprotectant can prevent morphological changes of the dispersion particles in the formulation during lyophilization. The formulation can be easily dispersed in water, by simple-shaking process, without requiring any strong mechanical force. Hence, the constituting ingredients and the pharmaceutical compound in the dispersed particles are not degraded. The formulations efficiently provides improved drug delivery system, as they effectively exhibit sustained drug release characteristics. All the raw materials in the formulation are biocompatible, and hence is efficiently utilized in medical and pharmaceutical fields. The formulations can be stored at room temperature in a sealed state for prolonged period, without undergoing phase separation or change in properties of the formulations, as the powder formulation does not contact with organic solvent or moisture. The lyophilized liquid and powder compositions, are physiochemically stable, as they does not contain water that causes oxidation or hydrolysis upon storage.

Dwg.0/2

L13 ANSWER 10 OF 21 EMBASE on STN

ACCESSION NUMBER: 2001341072 EMBASE

TITLE: Intestinal drug efflux: Formulation and food effects.
AUTHOR: Wagner D.; Spahn-Langguth H.; Hanafy A.; Koggel A.; Langguth P.
CORPORATE SOURCE: P. Langguth, Department Pharmaceutical Technology, School of Pharmacy, Johannes Gutenberg-University, Staudingerweg 5, 55099 Mainz, Germany. langguth@mail.uni-mainz.de
SOURCE: Advanced Drug Delivery Reviews, (1 Oct 2001) 50/SUPPL. 1 (S13-S31). Refs: 87
ISSN: 0169-409X CODEN: ADDREP
PUBLISHER IDENT.: S 0169-409X(01)00183-1
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The intestine, primarily regarded as an absorptive organ, is also prepared for the elimination of certain organic acids, bases and neutral compounds depending on their affinity to intestinal carrier systems. Several of the transport systems known to mediate efflux in the major clearing organs - liver and kidney - are also expressed in the intestine. Examples of secretory transporters in the intestine are P-glycoprotein, members of the multidrug resistance associated protein family, breast cancer resistance protein, organic cation transporters and members of the organic anion polypeptide family. In this communication, the P-glycoprotein mediated intestinal secretion of talinolol, a model compound showing metabolic stability, has been investigated in the jejunum, ileum and colon of rat intestine by single-pass perfusion. A model has been developed which demonstrates an increase in carrier-mediated secretion in the order jejunum < ileum < colon. Furthermore, the potency of common excipients in peroral drug products towards inhibition of P-gp mediated secretion has been investigated using a radioligand-binding assay and transport studies in Caco-2 cell monolayers. Finally, evidence is provided which demonstrates that constituents of grapefruit juice not only may influence intestinal drug metabolism, but can also interfere with secretory transport systems, leading to a new and yet undescribed mechanism in drug-food interactions. .COPYRGT. 2001 Elsevier Science B.V. All rights reserved.

L13 ANSWER 11 OF 21 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-587382 [55] WPIDS
DOC. NO. CPI: C2000-175197
TITLE: Pharmaceutical composition containing **cyclosporin** together with organic acids, fish oil and optional water, for use to prevent rejection of organ transplant and bone marrow transplant and to treat autoimmune diseases.
DERWENT CLASS: B03
INVENTOR(S): ZHANG, Y
PATENT ASSIGNEE(S): (ZHON-N) ZHONGMEI HUADONG PHARM CO LTD HANGZHOU; (HANG-N) HANGZHOU ZHONGMEI HUADONG PHARM CO LTD
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000053212	A1	20000914	(200055)*	ZH	21

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

CN 1265920	A	20000913	(200062)
AU 2000027927	A	20000928	(200067)
GB 2363572	A	20020102	(200203)
BR 2000010454	A	20020108	(200208)
KR 2001112315	A	20011220	(200239)
DE 10084344	T	20020711	(200253)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000053212	A1	WO 2000-CN41	20000302
CN 1265920	A	CN 1999-102848	19990309
AU 2000027927	A	AU 2000-27927	20000302
GB 2363572	A	WO 2000-CN41	20000302
		GB 2001-21845	20010910
BR 2000010454	A	BR 2000-10454	20000302
		WO 2000-CN41	20000302
KR 2001112315	A	KR 2001-711483	20010910
DE 10084344	T	DE 2000-10084344	20000302
		WO 2000-CN41	20000302

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000027927	A	Based on	WO 2000053212
GB 2363572	A	Based on	WO 2000053212
BR 2000010454	A	Based on	WO 2000053212
DE 10084344	T	Based on	WO 2000053212

PRIORITY APPLN. INFO: CN 1999-102848 19990309

AN 2000-587382 [55] WPIDS

AB WO 200053212 A UPAB: 20001130

NOVELTY - A **cyclosporin**-containing drug composition comprises:

(1) a **cyclosporin**;

(2) **ethanol** and/or glycerol;

(3) a hydrophilic surfactant;

(4) medium or long-chain (un)saturated fatty acids and/or substituted carboxylic acids, or fish oil; and

(5) water.

DETAILED DESCRIPTION - A **cyclosporin**-containing drug composition comprises:

(1) **cyclosporin** as active ingredient;

(2) **ethanol** an/or glycerol, as solvent or surface-active auxiliary;

(3) a hydrophilic surfactant with HLB (hydrophile-lyophile balance) value of 10-19 as solubilizer;

(4) medium or long-chain (un)saturated fatty acids an/or substituted carboxylic acids, or fish oil as hydrophobic component;

(5) water as required to make a hydrophilic medium to give dosage forms like soft **capsules**, pastes, **eye drops**, **oral** liquids and **injection** solutions.

ACTIVITY - Immunosuppressive.

MECHANISM OF ACTION - None given.

USE - The composition is useful for preventing rejection of organ transplant and bone marrow transplant and for treating autoimmune diseases.

ADVANTAGE - Such composition can provide higher stability and bioavailability.

Dwg.0/1

L13 ANSWER 12 OF 21 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-258599 [23] WPIDS
CROSS REFERENCE: 2000-239059 [20]
DOC. NO. CPI: C2000-079207
TITLE: Temperature stable **oral** composition of **cyclosporin**, suitable for use in tropical regions, comprises a hydrophilic carrier medium including **propylene glycol**, triacetin, and a vegetable oil triglyceride.
DERWENT CLASS: A96 B04
INVENTOR(S): JAIN, R; SINGH, A
PATENT ASSIGNEE(S): (PANA-N) PANACEA BIOTEC LTD
COUNTRY COUNT: 26
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 982035	A1	20000301	(200023)*	EN	20
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
SG 78314	A1	20010220	(200123)#		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 982035	A1	EP 1998-306607	19980818
SG 78314	A1	SG 1998-3610	19980911

PRIORITY APPLN. INFO: EP 1998-306607 19980818; SG 1998-3610 19980911
AN 2000-258599 [23] WPIDS
CR 2000-239059 [20]
AB EP 982035 A UPAB: 20010425
NOVELTY - A homogeneous substantially alcohol free, transparent **cyclosporin** solution, in a hydrophilic carrier medium, is new. The solution is clear, stable, flowable and easily measured at 15-45 deg. C. The medium comprises **propylene glycol**, a natural vegetable oil triglyceride and polyalkylene polyol transesterification product, a polyoxyethylene hydrogenated castor oil product, and triacetin.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included

for an improved process for making soft gelatin **capsules**, containing the novel composition, comprising adding 10-25% excess of the base carrier medium, to the composition, to compensate for weight loss due to free hydroxy group migration with the **capsule** shell. This prevents drug precipitation due to solvent loss, and substantially reduces from the **capsule** shell, 10-25% of the polyols, such as sorbitol and glycerol, which are used as plasticizers.

ACTIVITY - Immunosuppressant

MECHANISM OF ACTION - None given.

USE - The composition is used to provide an **oral** administration of the immunosuppressant **cyclosporin**, which is stable at up to 45 deg. C (claimed).

ADVANTAGE - The **cyclosporin** composition is stable at temperatures up to 45 deg. C, meaning that it can be used in tropical regions which have high temperatures, and lack refrigeration or air conditioning systems. The **capsular** form is easy to carry and simple to administer.

Dwg.0/0

L13 ANSWER 13 OF 21 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-468614 [39] WPIDS
CROSS REFERENCE: 1997-192527 [16]; 1997-489384 [45]
DOC. NO. CPI: C1999-137368
TITLE: **Oral cyclosporin** formulation for immunosuppressive therapy.
DERWENT CLASS: A25 A96 B04
INVENTOR(S): CHU, M J; LEVY, R E; POULETTY, P J; CHO, M J
PATENT ASSIGNEE(S): (SANG-N) SANGSTAT MEDICAL CORP; (UYNC-N) UNIV NORTH CAROLINA
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9920296	A1	19990429	(199939)*	EN	35
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9898106	A	19990510	(199939)		
ZA 9809684	A	19990728	(199939)		30
NO 9903096	A	19990817	(199944)		
US 5962019	A	19991005	(199948)		
EP 956035	A1	19991117	(199953)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
CZ 9902337	A3	20000112	(200009)		
CN 1246057	A	20000301	(200029)		
BR 9806271	A	20000404	(200030)		
JP 2000516267	W	20001205	(200067)		36
MX 9905830	A1	19991001	(200103)		
KR 2000069688	A	20001125	(200130)		
HU 2000004733	A2	20010528	(200140)		
NZ 336253	A	20010629	(200140)		
RU 2174405	C2	20011010	(200175)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9920296	A1		WO 1998-US22330	19981021
AU 9898106	A		AU 1998-98106	19981021
ZA 9809684	A		ZA 1998-9684	19981023
NO 9903096	A		WO 1998-US22330	19981021
			NO 1999-3096	19990622
US 5962019	A	CIP of	US 1995-519689	19950825
		CIP of	US 1996-620021	19960321
			US 1997-956841	19971023
EP 956035	A1		EP 1998-952393	19981021
			WO 1998-US22330	19981021
CZ 9902337	A3		WO 1998-US22330	19981021
			CZ 1999-2337	19981021
CN 1246057	A		CN 1998-801568	19981021
BR 9806271	A		BR 1998-6271	19981021
			WO 1998-US22330	19981021
JP 2000516267	W		WO 1998-US22330	19981021
			JP 1999-524568	19981021
MX 9905830	A1		MX 1999-5830	19990621
KR 2000069688	A		WO 1998-US22330	19981021
			KR 1999-705738	19990623
HU 2000004733	A2		WO 1998-US22330	19981021
			HU 2000-4733	19981021
NZ 336253	A		NZ 1998-336253	19981021
			WO 1998-US22330	19981021
RU 2174405	C2		WO 1998-US22330	19981021
			RU 1999-113343	19981021

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9898106	A	Based on	WO 9920296
US 5962019	A	CIP of	US 5766629
		CIP of	US 5834017
EP 956035	A1	Based on	WO 9920296
CZ 9902337	A3	Based on	WO 9920296
BR 9806271	A	Based on	WO 9920296
JP 2000516267	W	Based on	WO 9920296
KR 2000069688	A	Based on	WO 9920296
HU 2000004733	A2	Based on	WO 9920296
NZ 336253	A	Based on	WO 9920296
RU 2174405	C2	Based on	WO 9920296

PRIORITY APPLN. INFO: US 1997-956841 19971023; US 1995-519689 19950825; US 1996-620021 19960321

AN 1999-468614 [39] WPIDS

CR 1997-192527 [16]; 1997-489384 [45]

AB WO 9920296 A UPAB: 20011220

NOVELTY - **Oral cyclosporin** formulation comprises **cyclosporin,** 2-3C alkanol, nonionic polyoxyalkylene surfactant and polyglycol.

DETAILED DESCRIPTION - **Oral cyclosporin** formulation comprises:

(1) **cyclosporin;**

(2) at least one 2-3C alkanol solvent;

(3) at least one nonionic polyoxyalkylene surfactant comprising polyoxyethylene alcohols and 4-6C fatty acid monoesters of ethoxylated polyols and

(4) at least one polyglycol, in which at least one polyglycol has a molecular weight of 800-1000 daltons.

An INDEPENDENT CLAIM is included for an **oral** anhydrous **cyclosporin** formulation comprising **cyclosporin** and a carrier.

ACTIVITY - Immunosuppressive.

A **cyclosporin** formulation comprised: **cyclosporin** A (100 mg; 10% w/v), **ethanol** (0.1 ml, 10%), **Tween** 80 (300 mg; 0.278 ml) and isopropyl myristate (0.622 ml; 531 mg; qs to 1.0 ml). Greater bioavailability of **cyclosporin** was achieved with the formulation as compared with SANDIMMUNE (RTM) **oral** solution.

MECHANISM OF ACTION - None given.

USE - Used in immunosuppressive therapy including the treatment of idiopathic nephrotic syndrome, type 1 insulin-dependent diabetes, Behcet's syndrome, active Crohn's disease, aplastic anaemia, severe corticosteroid-dependent asthma, psoriasis, rheumatoid arthritis and graft versus host disease e.g. following bone marrow transplantation.

ADVANTAGE - The **oral cyclosporin** formulation has high bioavailability which reduces precipitation of **cyclosporin** from the formulation.

Dwg.0/6

L13 ANSWER 14 OF 21 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1996-231901 [24] WPIDS
DOC. NO. CPI: C1996-073381
TITLE: Storage-stable **cyclosporin** soft **capsule** compsn - contg di methyl isosorbide, oil component and surfactant giving high bio-availability, used e.g. as immunosuppressant.
DERWENT CLASS: A96 B04 B07 C03 C07
INVENTOR(S): WOO, J S; WOO, J
PATENT ASSIGNEE(S): (HANM-N) HANMI PHARM IND CO LTD; (KARA-N) KARAMI YAKUHIN KOGYO KK; (NOVS) NOVARTIS AG
COUNTRY COUNT: 9
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 711550	A1	19960515	(199624)*	EN	25
R: BE DE FR GB IT					
JP 08310964	A	19961126	(199706)		14
US 5603951	A	19970218	(199713)		11
CN 1128671	A	19960814	(199750)		
KR 167696	B1	19990115	(200038)		
EP 711550	B1	20020116	(200212)	EN	
R: BE DE FR GB IT					
DE 69525019	E	20020221	(200221)		
JP 3391961	B2	20030331	(200325)		14

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 711550	A1	EP 1995-117171	19951031
JP 08310964	A	JP 1995-291336	19951109
US 5603951	A	US 1995-427190	19950421
CN 1128671	A	CN 1995-118554	19951030
KR 167696	B1	KR 1995-37618	19951027
EP 711550	B1	EP 1995-117171	19951031
DE 69525019	E	DE 1995-625019	19951031
		EP 1995-117171	19951031
JP 3391961	B2	JP 1995-291336	19951109

FILING DETAILS:

PATENT NO	KIND		PATENT NO
DE 69525019	E	Based on	EP 711550
JP 3391961	B2	Previous Publ.	JP 08310964

PRIORITY APPLN. INFO: KR 1994-29208 19941109

AN 1996-231901 [24] WPIDS

AB EP 711550 A UPAB: 19960829

A **cyclosporin** soft **capsule** compsn. comprises: (A) a **cyclosporin** (pref. **cyclosporin** A) as active ingredient; (B) dimethyl isosorbide as cosurfactant; (C) at least one of fatty acid/prim. alcohol esters, medium chain fatty acid triglycerides and fatty acid monoglycerides as oil component; and (D) a surfactant having HLB value 10-17.

Pref. (D) is polyoxyethylene hydrogenated vegetable oil or polyoxyethylene sorbitan fatty acid ester, pref. a mixture of `Nikkol HCO-50' (RTM); POE (50) hydrogenated castor oil) and `**Tween** 20' (RTM; POE (20) sorbitan monolaurate).

USE - (A) have immunosuppressant and antiinflammatory activity, and are used for suppressing immune response to tissue and organ transplants. They are also used for treating haematological disorders (e.g. anaemia), autoimmune disorders (e.g. systemic lupus erythematosus or idiopathic maladsorption syndrome), inflammatory disorders (e.g. arthritis or rheumatism) and protozoal diseases (e.g. malaria or schistosomiasis); and in chemotherapy.

ADVANTAGE - When formulated in a soft **capsule**, the compsn. is more storage-stable and remains uniform for a longer period than conventional **ethanol**-based compsns. such as `Sandimmun' (RTM). The compsn. also provides high bioavailability and less variation in blood levels between patients. (B) is non-volatile, does not penetrate gelatin **capsule** shells, is non-hygroscopic and readily dissolves (A).

Dwg.0/3

ABEQ US 5603951 A UPAB: 19970326

A **cyclosporin** soft **capsule** composition comprising **cyclosporin** as an active ingredient, dimethylisosorbide as co-surfactant, one or more components selected from the group consisting of an esterified compound of fatty acid and primary alcohol, medium chain fatty acid triglyceride and fatty acid monoglyceride as an oil component, and a surfactant having an HLB (Hydrophilic-lipophilic balance) value of 10 to 17.

Dwg.0/3

L13 ANSWER 15 OF 21 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1995-231360 [30] WPIDS
DOC. NO. CPI: C1995-106782
TITLE: Pharmaceutical compsn. containing alkyl polyoxyalkylene carboxylate - for enhancing solubility of the active agent.
DERWENT CLASS: A96 B04 B05 B07
INVENTOR(S): AU, S Y; BAUMANN, W K; NAZARENO, J P; SHARKEY, J W
PATENT ASSIGNEE(S): (SANO) SANDOZ LTD; (SANO) SANDOZ PATENT GMBH; (SANO) SANDOZ-ERFINDUNGEN VERW GES MBH
COUNTRY COUNT: 56
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9516465	A1	19950622	(199530)*	EN	23
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ					
W: AM AU BB BG BR BY CA CN CZ FI GE HU JP KE KG KP KR KZ LK LT LV MD MG MN MW NO NZ PL RO RU SD SI SK TJ TT UA UZ VN					
AU 9513136	A	19950703	(199542)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9516465	A1	WO 1994-EP4128	19941213
AU 9513136	A	AU 1995-13136	19941213

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9513136	A	Based on	WO 9516465

PRIORITY APPLN. INFO: US 1993-167254 19931214
AN 1995-231360 [30] WPIDS
AB WO 9516465 A UPAB: 19950804
Pharmaceutical compsn. comprises one or more pharmaceutically active agents and one or more alkyl polyoxyalkylene carboxylate esters of the formula (I): R is 8-22C alkyl; R1 is 1-22C alkyl; m is 0-4; n is 3-20; o is 1-4; p is 0-20. With proviso that when, (i) R1 is 1-3C alkyl; then p is zero; and (ii) m is zero; then n is 6-20.

Pref. (I) is a mixture of isopropyl 12-15C pareth-9-carboxylates or a mixture of isopropyl polypropylene, glycol-2-isodeceth-7-carboxylates. The amount of (I) is pref. 5-20 weight % based on the total compsn. weight Pref. there is additionally present a hydrophilic solvent e.g. water, an alcohol or in aqueous alcohol, especially water and/or **ethanol**. The compsn. may be in a form for **oral**, topical or transdermal application.

USE - (I) enhance the solubility of the active agent and hence increase its bioavailability. Thus, the bioavailability through in vitro skin permeation of terbinafine (antifungal agent) at 8 mg/ml in water containing 10 weight% of isopropyl 12-15C pareth-9-carboxylate is substantially increased compared with the agent in water containing **Tween** (RTM) 20 in place of the cpd. (I). Terbinafine and its salts are preferred active agents and others are **cyclosporins**, especially **cyclosporin** A, but a long life

of active agents is given including local anaesthetics, narcotic analgesics, non-narcotic analgesics, antibacterials and antibiotics, antifungals, land anti-inflammatory agents. The compsn. is especially useful and beneficial with agents which are substantially insoluble in water at 22deg.C.
Dwg.0/1

L13 ANSWER 16 OF 21 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 95287351 EMBASE
DOCUMENT NUMBER: 1995287351
TITLE: Atherogenic effects of **cyclosporine** in an experimental model of arterial autograft.
AUTHOR: Bellon J.M.; Bujan M.J.; Jurado F.; Hernando A.; Ga-Honduvilla N.; Dominguez B.; Contreras L.
CORPORATE SOURCE: Morphological Sciences/Surgery Dept., Faculty of Medicine, Carret N-II,28871 Alcala de Henares, Madrid, Spain
SOURCE: Transplantation, (1995) 60/5 (407-414).
ISSN: 0041-1337 CODEN: TRPLAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB One of the effects attributed to CsA is a possible acceleration of atherogenic processes, which contributes to the failure of transplanted organs. This study was undertaken to evaluate the effect of CsA and two vehicles, cremophor and **ethanol**, in an experimental model of arterial autograft in the rat. Female Sprague-Dawley rats were distributed into 3 study groups: Group 1 (control) had an arterial autograft in the common iliac artery without pretreatment; group 2 (CsA-cremophor) animals were pretreated with a daily dose of CsA (5 mg/kg, Sandimmun) for 4 days before the autograft was made; and group 3 (CsA-**ethanol** + **Tween**) animals were pretreated for 4 days before implantation of the autograft with CsA in a vehicle of **ethanol** + **Tween** at the same dose as used in group 2 (5 mg/kg). The study periods were 7, 14, 21, 30, and 50 postoperative days. Studies were made by optical microscopy, transmission electron microscopy, scanning electron microscopy, and autoradiography. Evaluation of the results showed that in the control group the postoperative repair process lead to formation of an intimal neolayer throughout the entire surgical zone, with scant participation of white cells. Group 2 (CsA-cremophor) had a marked increase in luminal thrombogenicity, important adhesion and infiltration of white cells, loss of smooth muscle cells in the medial layer, and atherogenic degeneration of the medial layer. The generation of the neointimal layer is delayed by 2 weeks with respect to the control group. However, once the neointimal begins to form, its thickness increases rapidly, reaching values similar to those seen in the control group at 50 days. The myointima also shows atherogenic characteristics, such as monocyte-macrophage infiltration and dystrophic calcification. In group 3 (CsA-

ethanol + **Tween**, that is, CsA in a nonoleaginous vehicle), the effects were similar to those seen in group 2 (CsA-cremophor), with a reduction in the presence of lipid-laden cells in the medial layer. Based on these observations, we conclude that CsA per se induced atherogenic changes in the repair process of the arterial lesion that were independent of the vehicle of administration. CsA delayed, but did not inhibit, formation of a myointima and the myointima formed exhibited atherogenic characteristics. The most important effects were noted in the medial layer, which experienced intense degeneration.

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ACCESSION NUMBER:	95003046 EMBASE
DOCUMENT NUMBER:	1995003046
TITLE:	Nephrotoxity of FK 506: A preliminary study on comparative aspects of FK 506 and **cyclosporine** nephrotoxicity.
AUTHOR:	Nielsen F.T.; Leyssac P.P.; Kemp E.; Starklint H.; Dieperink H.
CORPORATE SOURCE:	Department of Nephrology 'Y', Odense University Hospital,DK-5000 Odense C, Denmark
SOURCE:	Transplantation Proceedings, (1994) 26/6 (3104-3105). ISSN: 0041-1345 CODEN: TRPPA8
COUNTRY:	United States
DOCUMENT TYPE:	Journal; Conference Article
FILE SEGMENT:	026 Immunology, Serology and Transplantation 028 Urology and Nephrology 030 Pharmacology 037 Drug Literature Index 052 Toxicology
LANGUAGE:	English

L13 ANSWER 18 OF 21 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER:	93203486 EMBASE
DOCUMENT NUMBER:	1993203486
TITLE:	Leaching of diethylhexyl phthalate from polyvinyl chloride containers by selected drugs and formulation components.
AUTHOR:	Pearson S.D.; Trissel L.A.
CORPORATE SOURCE:	Division of Pharmacy, Texas Univ. M. D. Anderson Can. Ctr., Box 90, 1515 Holcombe Boulevard,Houston, TX 77030, United States
SOURCE:	American Journal of Hospital Pharmacy, (1993) 50/7 (1405-1409). ISSN: 0002-9289 CODEN: AJHPA
COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article
FILE SEGMENT:	017 Public Health, Social Medicine and Epidemiology 030 Pharmacology 036 Health Policy, Economics and Management 037 Drug Literature Index
LANGUAGE:	English
SUMMARY LANGUAGE:	English

AB The extent of leaching of diethylhexyl phthalate (DEHP) from polyvinyl chloride (PVC) bags by several organic solvents and

surfactants used as formulation components and by 12 drug products containing these solvents and surfactants was studied. The organic solvents **ethanol**, polyethylene glycol, and **propylene glycol**, the surfactants polysorbate 80 and polyoxyethylated castor oil, and the 12 drugs were admixed separately in PVC bags of 5% dextrose **injection**. At the time of preparation and after 4, 8, and 24 hours at 24°C, the concentration of DEHP in duplicate samples was determined in duplicate by high-performance liquid chromatography. **Ethanol**, polyethylene glycol, and **propylene glycol** at concentrations of 25% and the drugs containing these components did not leach DEHP within the study period. Polysorbate 80 1% to 25% leached detectable amounts of DEHP in as little as one hour at the high concentration and within four hours at the lower concentrations; at 24 hours, DEHP concentrations ranged from 36 µg/mL for 1% polysorbate 80 to 237 µg/mL for 25% polysorbate 80. Similar results were observed for polysorbate 80 plus **ethanol** and for polyoxyethylated castor oil plus **ethanol**. Drug products containing surfactants, including **cyclosporine**, miconazole, and teniposide, and the vehicles used in formulating taxol and taxotere, leached relatively large amounts of DEHP in 24 hours. Smaller amounts were leached by chlordiazepoxide hydrochloride and etoposide. DEHP was leached from PVC containers by a variety of surfactants and drug products containing these surfactants. Drugs that leach DEHP should be prepared in non-PVC containers and administered through non-PVC tubing.

L13 ANSWER 19 OF 21 JICST-EPlus COPYRIGHT 2003 JST on STN

ACCESSION NUMBER: 920147788 JICST-EPlus

TITLE: Experimental Studies on Vascularized Allogeneic Joint Graft. 7th. Report. Effects of the Difference of Histocompatibility Antigen on Grafted Joint Treated with **Cyclosporin** A.

AUTHOR: ITOGA HIDEYA; MINAMI AKIO; KOBAYASHI MASAYUKI TAKAHARA MASATOSHI

CORPORATE SOURCE: Hokkaido Univ., School of Medicine
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SOURCE: Nippon Te no Geka Gakkai Zasshi (Journal of Japanese Society for Surgery of the Hand), (1991) vol. 8, no. 3, pp. 527-530. Journal Code: X0154A (Fig. 1, Tbl. 2, Ref. 11)
ISSN: 0910-5700

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Article

LANGUAGE: Japanese

STATUS: New

AB Our previous experimental studies were designed to investigate the influence of subregions of major histocompatibility (RT1) antigen in rat on survival of grafted joint. These sutdies suggested that the success of the vascularized allogeneic joint transplantation was depend on the low antigenicity of the transplanted joint. But even if one or two subregions of RT1 were matched between donor and recipient rats, the grafted joint finally rejected. So in this paper the effect of subregions of RT1-on rat joint transplant prolongation is investigated under the short-term and low-dose administration of **Cyclosporine**. Four strains of an inbred rat were used for

vascularized joint transplantation. The rats were classified into three groups according to the difference of subregions of the RT1 antigen between donor and recipient rats; Group I: RT1-A, B, D barrier (from WKA to LEJ rats), Group II: RT1-B, D barrier (from To to LEJ rats), Group III: RT1-Abarrier (from BUF to LEJ rats). **Cyclosporin** was solubilized (25mg/ml) using 20% **Tween** 80 in anhydrous **ethanol**, and was given 10mg/kg day for 14 days posttransplantation by s.c. **injection**. Appearance of the transplanted limb; survival, edema or necrosis was observed macroscopically. Histological studies were also performed. The transplanted limb in Group I became edematous at an average of 22 days and followed limb necrosis at 41 days after the transplantation. On the other hand, in Group II and Group III the transplanted limbs became edematous at 41 days and 40 days, but necrosis was not observed. (abridged author abst.)

L13 ANSWER 20 OF 21 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 90189676 MEDLINE
DOCUMENT NUMBER: 90189676 PubMed ID: 2314004
TITLE: **Cyclosporin** reduces renal blood flow through vasoconstriction of arcuate arteries in the hydronephrotic rat model.
AUTHOR: Zimmerhackl L B; Fretschner M; Steinhausen M
CORPORATE SOURCE: Kinderklinik der Universitat Freiburg.
SOURCE: KLINISCHE WOCHENSCHRIFT, (1990 Feb 1) 68 (3) 166-74. Journal code: 2985205R. ISSN: 0023-2173.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199004
ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 19900601
Entered Medline: 19900425

AB Besides its beneficial effects in organ transplantation **cyclosporin** (CyA) exhibits nephrotoxic (and other) side effects. CyA nephrotoxicity is associated with a decrease in glomerular filtration rate. Two mechanisms of action have emerged. First, tubular destruction with secondary reduction in renal blood flow and glomerular filtration rate; second, decrease in renal blood flow with secondary interstitial fibrosis. We studied the effect of an acute infusion of CyA in the hydronephrotic rat kidney model, which lacks tubular structures completely. Hence, only the direct vascular effects of CyA were determined. Five groups (G) of rats were studied by television microscopy. G I (n = 7) received CyA (30 mg/kg, **i.v.**) dissolved in cremophore/plasma; G II (n = 5), time control 1, received cremophore/plasma instead of CyA; G III (n = 8), received CyA 30 mg/kg followed by 20 mg/kg CyA **i.v.** dissolved in an **ethanol**/**tween** solution; G **IV** (n = 3), time control 2 received **ethanol**/**tween** alone in the experimental period; in G V, CyA was applied locally onto the surface of the kidney with concentrations increasing from 10(-7) to 10(-5) M. CyA caused profound reduction in the diameter of arcuate arteries in groups I and III, in contrast to the time control groups II and **IV**. The vasoconstriction could be partially reversed by the calcium-channel blocker nitrendipine, and completely reversed with acetyl-choline. Glomerular blood flow decreased due to CyA and

could not be completely normalized by either drug. Increasing the dosage from 30 to 50 mg/kg was not associated with further reduction in blood flow. Local application of CyA (G V) did not demonstrate vasoconstriction.(ABSTRACT TRUNCATED AT 250 WORDS)

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ACCESSION NUMBER: 80211900 EMBASE
DOCUMENT NUMBER: 1980211900
TITLE: **Cyclosporin** A prolongation of segmental pancreatic and islet allograft function in rats.
AUTHOR: Rynasiewicz J.J.; Sutherland D.E.R.; Kawahara K.; et al.
CORPORATE SOURCE: Dept. Surg., Univ. Minnesota Hlth Sci. Cent., Minneapolis, Minn. 55455, United States
SOURCE: Transplantation Proceedings, (1980) 12/2 (270-274). CODEN: TRPPA8
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
026 Immunology, Serology and Transplantation
048 Gastroenterology
LANGUAGE: English

(FILE 'MEDLINE' ENTERED AT 15:54:51 ON 22 OCT 2003)

L14 15874 SEA FILE=MEDLINE ABB=ON PLU=ON CYCLOSPORINE/CT
L15 46597 SEA FILE=MEDLINE ABB=ON PLU=ON ETHANOL/CT
L16 643 SEA FILE=MEDLINE ABB=ON PLU=ON "PROPYLENE GLYCOL"/CT
L17 20 SEA FILE=MEDLINE ABB=ON PLU=ON L14 AND (L15 OR L16)
L18 5354 SEA FILE=MEDLINE ABB=ON PLU=ON CAPSULES/CT
L19 70156 SEA FILE=MEDLINE ABB=ON PLU=ON "ADMINISTRATION, ORAL"/CT
L20 7514 SEA FILE=MEDLINE ABB=ON PLU=ON OINTMENTS/CT
L21 7045 SEA FILE=MEDLINE ABB=ON PLU=ON "OPHTHALMIC SOLUTIONS"/CT
L22 20658 SEA FILE=MEDLINE ABB=ON PLU=ON INJECTIONS/CT
L23 1 SEA FILE=MEDLINE ABB=ON PLU=ON L17 AND (L18 OR L19 OR L20 OR L21 OR L22)

L23 ANSWER 1 OF 1 MEDLINE on STN
AN 1999253456 MEDLINE
TI Toxicological evaluation of cyclosporine eyedrops.
AU Knagenhjelm S K; Froyland K; Ringvold A; Bjerkas E; Kjonniksen I
SO ACTA OPHTHALMOLOGICA SCANDINAVICA, (1999 Apr) 77 (2) 200-3. Journal code: 9507578. ISSN: 1395-3907.
AB PURPOSE: The short-term toxicological effects of two cyclosporine A eyedrop formulations are compared. METHODS: Formula A was based on Sandimmune (Novartis, Switzerland) infusion concentrate with a final ethanol concentration of 1% (w/w), and formula B on Sandimmune oral solution. Both formulations were diluted in sterile peanut oil (10 mg/ml). The left eyes of 12 rabbits were treated with the cyclosporine eyedrops over a two-week period. The right eyes served as controls. Slit-lamp and scanning electron microscopic examinations were performed, and the total protein concentration in aqueous humor was measured in treated and control eyes. RESULTS AND CONCLUSION: Both Sandimmune oral solution and infusion concentrate-derived eyedrops were found to be non-toxic to rabbit eyes and there were no significant differences between the two

formulations. More definite conclusions as to the safety of these cyclosporine formulations cannot be made without long-term trials.

L24 19 S L17 NOT L23

L24 ANSWER 1 OF 19 MEDLINE on STN
AN 2001433478 MEDLINE
TI The mitochondrial permeability transition contributes to acute ethanol-induced apoptosis in rat hepatocytes.
AU Higuchi H; Adachi M; Miura S; Gores G J; Ishii H
SO HEPATOLOGY, (2001 Aug) 34 (2) 320-8.
Journal code: 8302946. ISSN: 0270-9139.
AB Acute ethanol intoxication induces oxidative stress and apoptosis in primary cultured hepatocytes. Oxidative stress can trigger mitochondrial cytochrome c release initiating the mitochondrial pathway of apoptosis. Based on this information, we formulated the hypothesis that ethanol induced oxidative stress causes mitochondrial dysfunction resulting in apoptosis. In the present study, we found that the mitochondrial membrane permeability transition (MPT) is essential for induction of mitochondrial cytochrome c release and caspase activation of ethanol. The short-term incubation with ethanol (50 mmol/L) induced the MPT, cytochrome c release, caspase activation, and apoptosis of cultured rat hepatocytes. Hepatocyte apoptosis was prevented by caspase inhibitors (i.e., Z-VAD-fmk, DEVD-cho, and DMQD-cho). An MPT inhibitor, cyclosporin A, also prevented ethanol-induced cytochrome c release, caspase activation, and apoptosis, suggesting that acute ethanol-induced apoptosis is MPT dependent. Ethanol-induced MPT was also attenuated by N'N'-dimethylthiourea (DMTU, a scavenger of hydrogen peroxide, 10 mmol/L) and N-acetyl-cysteine (NAC, an antioxidant, 5 mmol/L). Preventing hepatocyte MPT by DMTU or NAC attenuated cytochrome c release as well as caspase activation, suggesting that ethanol-induced oxidative stress mediates the MPT. Thus, acute ethanol induces MPT via oxidative stress, and the MPT mediates mitochondrial pathway of apoptosis in hepatocytes exposed to acute ethanol.

L24 ANSWER 2 OF 19 MEDLINE on STN
AN 2001369254 MEDLINE
TI Mitochondrial permeability transition induced by 1-hydroxyethyl radical.
AU Sakurai K; Stoyanovsky D A; Fujimoto Y; Cederbaum A I
SO FREE RADICAL BIOLOGY AND MEDICINE, (2000 Jan 15) 28 (2) 273-80.
Journal code: 8709159. ISSN: 0891-5849.
AB Impairment of mitochondrial functions has been found in ethanol-induced liver injury. Ethanol can be oxidized to the 1-hydroxyethyl radical (HER) by rat liver microsomal systems. Experiments were carried out to evaluate the ability of HER to cause mitochondrial swelling as an indicator of the mitochondrial permeability transition (MPT). Electron spin resonance (ESR) spectroscopy was used to detect HER and to study its interaction with mitochondria. The ESR signal intensity of the spin adduct formed from alpha-(4-pyridyl-1-oxide) N-tert-butylnitrone (POBN) and HER generated from either a thermic decomposition of 1,1'-dihydroxyazoethane (DHAE) or a Fenton reaction system containing ethanol was markedly diminished by the addition of mitochondria, indicating an interaction between HER and

mitochondria. Exposure of rat liver mitochondria to HER generated from either system caused swelling, as reflected by a decrease in absorbance at 540 nm, in a HER concentration-dependent and a cyclosporin A-sensitive manner. Mitochondrial swelling was also induced in the Fenton reaction system without ethanol. The DHAE-dependent generation of HER in mitochondrial suspension resulted in a decrease of membrane protein thiols and collapse of the membrane potential (delta psi). The swelling induced by HER was prevented by glutathione and vitamin E, but not by superoxide dismutase. Catalase did not prevent the swelling caused by the acetaldehyde/hydroxylamine O-sulfonate (HOS) system, but was inhibitory in the Fenton reaction system with or without ethanol. These results indicate that HER, as well as hydroxyl radical, can induce the MPT, and suggest the possibility that the collapse of delta psi caused by HER may, at least in part, contribute to impairment of mitochondrial function caused by ethanol and in ethanol-induced liver injury.

L24 ANSWER 3 OF 19 MEDLINE on STN
AN 2000257984 MEDLINE
TI Ethanol potentiates tumor necrosis factor-alpha cytotoxicity in hepatoma cells and primary rat hepatocytes by promoting induction of the mitochondrial permeability transition.
AU Pastorino J G; Hoek J B
SO HEPATOLOGY, (2000 May) 31 (5) 1141-52.
Journal code: 8302946. ISSN: 0270-9139.
AB In the present study, tumor necrosis factor-alpha (TNF-alpha) cytotoxicity is shown to be potentiated by ethanol exposure in vitro in the human hepatoma cell line, HepG2, and in rat primary hepatocytes. Exposure of HepG2 cells and primary hepatocytes for 48 hours to concentrations of ethanol ranging between 50 and 100 mmol/L significantly increased TNF-alpha cytotoxicity compared with cells treated with TNF-alpha alone. The cell killing was associated with, and dependent on, the development of the mitochondrial permeability transition (MPT). Two inhibitors of MPT pore opening, cyclosporin A and bongkrekic acid, prevented TNF-alpha cytotoxicity in the presence of ethanol. In addition to inhibiting cell death caused by TNF-alpha, blockade of MPT pore opening prevented mitochondrial depolarization, cytochrome c redistribution from the mitochondria to the cytosol, caspase 3 activation, and oligonucleosomal DNA fragmentation. Unlike the potentiation of TNF-alpha cytotoxicity by the translational inhibitor cycloheximide, ethanol promoted TNF-alpha-induced cell killing by a mechanism that was independent of caspase-8 activity. HepG2 cells overexpressing cytochrome-P4502E1 were even more sensitized by ethanol to induction of the MPT by TNF-alpha and the resultant cytotoxicity than wild-type HepG2 cells. In addition, primary hepatocytes isolated from chronically ethanol-fed rats showed enhanced susceptibility to TNF-alpha cytotoxicity compared with their isocalorically matched controls. Again as with the HepG2 cells, inhibiting MPT pore opening prevented the cytotoxicity of TNF-alpha in the primary hepatocytes isolated from ethanol-fed animals.

L24 ANSWER 4 OF 19 MEDLINE on STN
AN 2000190083 MEDLINE
TI Immunosuppressive treatment affects cardiac and skeletal muscle mitochondria by the toxic effect of vehicle.
AU Sanchez H; Bigard X; Veksler V; Mettauer B; Lampert E; Lonsdorfer J;

Ventura-Clapier R
SO JOURNAL OF MOLECULAR AND CELLULAR CARDIOLOGY, (2000 Feb) 32 (2) 323-31.
Journal code: 0262322. ISSN: 0022-2828.
AB In order to examine whether immunosuppressive treatment could be responsible for the reduced exercise capacity of heart transplant recipients (HTR), we studied the effects of long-term immunosuppressive treatment with cyclosporin A (CsA) and its vehicle (2/3 cremophor and 1/3 alcohol diluted in olive oil) on in situ mitochondrial respiration of different muscles. Rats were fed for 3 weeks with 10 or 25 mg/kg/day CsA in its vehicle (CsA10 and CsA25 groups), or vehicle or H(2)O. Oxygen consumption rate was measured in saponin skinned fibers without (V(0)) and with ADP until maximal respiration (V(max)) was reached and K(M)for ADP as well as V(max)were calculated using non-linear fit of the Michaelis-Menten equation. In the cardiac muscle of the CsA25 group, V(0)and V(max)were decreased by immunosuppressive treatment respectively from 6.33+/-0.51 to 3.18+/-0.3micromol O(2)/min/g dw (P<0.001) and from 29.0+/-1.5 to 18.1+/-1.6micromol O(2)/min/g dw (P<0.001), an effect which could be entirely attributed to the vehicle itself, with no difference between CsA10 and CsA25. Regulation of cardiac mitochondrial respiration by ADP was altered by vehicle with the K(M)for ADP decreasing from 371+/-37 to 180+/-21microm(P<0.001). A similar trend was observed in the diaphragm or soleus, although to a lesser extent. In contrast, V(0)and V(max)decreased in glycolytic gastrocnemius muscle respectively from 1.7+/-0.2 to 0.94+/-0.14 (P<0. 01) and from 6.8+/-0.3 to 5.1+/-0.4micromol O(2)/min/g dw (P<0.001) in the CsA25 group, but the main effects could be attributed to CsA itself. It was concluded that immunosuppressive treatment induces a deleterious effect on cardiac and skeletal muscle oxidative capacities, mainly due to cremophor, the main component of vehicle.

L24 ANSWER 5 OF 19 MEDLINE on STN
AN 2000025356 MEDLINE
TI Potentiation by chronic ethanol treatment of the mitochondrial permeability transition.
AU Pastorino J G; Marcineviciute A; Cahill A; Hoek J B
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1999 Nov 19) 265 (2) 405-9.
Journal code: 0372516. ISSN: 0006-291X.
AB Mitochondria isolated from rats chronically fed ethanol were more sensitive to induction of the mitochondrial permeability transition (MPT) by a variety of agents than mitochondria isolated from isocalorically matched controls. The agents utilized have been implicated in both necrotic (Ca(2+)) and apoptotic (ceramide, GD3 ganglioside, and Bax) forms of cell killing and help promote pore opening by differing mechanisms. In each case it was found that concentrations of the inducing agents which promoted little or no pore opening in mitochondria isolated from pair matched controls produced massive MTP opening in mitochondria from chronically ethanol fed rats as evidenced by swelling. In all cases induction of the MPT was prevented by the presence of cyclosporin A.

L24 ANSWER 6 OF 19 MEDLINE on STN
AN 1999241000 MEDLINE

TI Determination of cyclosporin A in 20% ethanol by a magnetic beads-based immunofluorescence assay.
AU Kiselev M V; Gladilin A K; Melik-Nubarov N S; Sveshnikov P G; Miethe P; Levashov A V
SO ANALYTICAL BIOCHEMISTRY, (1999 May 1) 269 (2) 393-8.
Journal code: 0370535. ISSN: 0003-2697.
AB A rapid magnetic beads-based immunoassay for the immunodepressant drug cyclosporin A (CsA) has been developed. The method allows CsA determination in medium with a higher content of ethanol compared to conventional immunochemical techniques due to increased antibody stability. Monitoring of the drug in ethanol extracts from patient's whole blood without many-fold dilution with aqueous buffer is possible. The assay has adequate specificity and sensitivity for CsA to be suitable for the routine monitoring of therapy.

L24 ANSWER 7 OF 19 MEDLINE on STN
AN 1998427827 MEDLINE
TI Biphasic effects of cyclosporin A on formyl-methionyl-leucyl-phenylalanine stimulated responses in HL-60 cells differentiated into neutrophils.
AU Nguyen N S; Pulido S M; Ruegg U T
SO BRITISH JOURNAL OF PHARMACOLOGY, (1998 Aug) 124 (8) 1774-80.
Journal code: 7502536. ISSN: 0007-1188.
AB The immunosuppressive drug cyclosporin A (CsA) depresses neutrophil oxidative burst which may lead to an increased susceptibility to infection in transplant patients. Using specific CsA analogues we investigated the mechanism of inhibition of the oxidative burst and evaluated short and long-term effects of CsA on dimethylsulphoxide-differentiated HL-60 neutrophils. A biphasic pattern was observed: a 4 h pre-treatment with CsA (1 microM) diminished the fMLP induced [Ca2+]c rise, reactive oxygen species (ROS) production, and beta-glucuronidase release by about 40%, whereas a 20 h pre-treatment increased these responses by about 1.5 fold. [MeVal4]CsA, which binds with high affinity to cyclophilin but inhibits the interaction of the CsA-cyclophilin complex with calcineurin, blocked the stimulation observed with CsA after a 20 h incubation but did not alter the CsA effects after a 4 h pre-treatment. PSC 833 (1 microM), a potent multi drug resistance transporter (MDR) inhibitor, diminished ROS production to the same extent as a 4 h CsA incubation but was ineffective after a 20 h pre-treatment. An involvement of MDR as a basis for CsA or PSC 833 action was ruled out based on the results of the calcein retention assay. [3H]CsA uptake showed that CsA and [MeVal4]CsA, but not CsH or PSC 833 were strongly taken up and retained by the cells. In conclusion, the reduction of the responses after 4 h appear to be due to a primary reduction of calcium signalling, while the enhanced responses after 20 h may be due to calcineurin inhibition.

L24 ANSWER 8 OF 19 MEDLINE on STN
AN 1998053167 MEDLINE
TI Mechanism of anaphylactoid reactions: improper preparation of high-dose intravenous cyclosporine leads to bolus infusion of Cremophor EL and cyclosporine.
AU Liau-Chu M; Theis J G; Koren G
SO ANNALS OF PHARMACOTHERAPY, (1997 Nov) 31 (11) 1287-91.
Journal code: 9203131. ISSN: 1060-0280.
AB BACKGROUND: During a Phase I/II trial of high-dose intravenous

cyclosporine, a high incidence of anaphylactoid reactions was observed. Epidemiologic investigations revealed that the occurrence of anaphylactoid reactions was significantly associated with improper mixing during preparation of the infusions. It was hypothesized that improper mixing during the preparation of the infusion may have caused initial bolus infusions of the vehicle, Cremophor EL. These inadvertent bolus infusions may have caused the anaphylactoid reactions. OBJECTIVE: To investigate the effect of different mixing techniques on the distribution of the components of cyclosporine concentrate for infusion: cyclosporine, Cremophor EL, and ethanol in the infusions administered to the patients. METHODS: Infusions were prepared in a similar fashion as those administered to study patients enrolled in a high-dose cyclosporine therapy protocol. Samples were collected at defined time points of the infusions. Concentrations of cyclosporine and Cremophor EL were spectrophotometrically determined; ethanol concentrations were measured enzymatically. RESULTS: Cyclosporine and Cremophor EL concentrations were up to ninefold higher than intended during the first 10 minutes of the infusions that were not appropriately mixed. In contrast, the concentrations of cyclosporine and Cremophor EL were similar to the intended concentrations in all of the well-mixed infusions. CONCLUSIONS: Inappropriate mixing of high-dose cyclosporine infusions can lead to initial bolus infusion of cyclosporine and Cremophor EL. Bolus infusions of Cremophor EL have been associated with anaphylactoid reactions. Thus, through mixing of high-dose cyclosporine infusions may be important to reduce the possibility of life-threatening anaphylactoid reactions.

L24 ANSWER 9 OF 19 MEDLINE on STN
AN 97407890 MEDLINE
TI Properties of a cyclosporin-insensitive permeability transition pore in yeast mitochondria.
AU Jung D W; Bradshaw P C; Pfeiffer D R
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Aug 22) 272 (34) 21104-12. Journal code: 2985121R. ISSN: 0021-9258.
AB Yeast mitochondria (Saccharomyces cerevisiae) contain a permeability transition pore which is regulated differently than the pore in mammalian mitochondria. In a mannitol medium containing 10 mM Pi and ethanol (oxidizable substrate), yeast mitochondria accumulate large amounts of Ca2+ (>400 nmol/mg of protein) upon the addition of an electrophoretic Ca2+ ionophore (ETH129). Pore opening does not occur following Ca2+ uptake, even though ruthenium red-inhibited rat liver mitochondria undergo rapid pore opening under analogous conditions. However, a pore does arise in yeast mitochondria when Ca2+ and Pi are not present, as monitored by swelling, ultrastructure, and matrix solute release. Pore opening is slow unless a respiratory substrate is provided (ethanol or NADH) but also occurs rapidly in response to ATP (2 mM) when oligomycin is present. Pi and ADP inhibit pore opening (EC50 approximately 1 and 4 mM, respectively), however, cyclosporin A (7 microg/ml), oligomycin (20 microg/ml), or carboxyatractyloside (25 microM) have no effect. The pore arising during respiration is also inhibited by nigericin or uncoupler, indicating that an acidic matrix pH antagonizes the process. Pi also inhibits pore opening by lowering the matrix pH (Pi/OH- antiport). However, inhibition of the ATP-induced pore by Pi is seen in the presence of mersalyl, suggesting a second mechanism of action. Since pore induction by ATP is not sensitive to carboxyatractyloside, ATP appears to act at

an external site and Pi may antagonize the interaction. Isoosmotic polyethylene glycol-induced contraction of yeast mitochondria swollen during respiration, or in the presence of ATP, is 50% effective at a solute size of 1.0-1.1 kDa. This suggests that the same pore is induced in both cases and is comparable in size with the permeability transition pore of heart and liver mitochondria.

L24 ANSWER 10 OF 19 MEDLINE on STN
AN 96119865 MEDLINE
TI Tyrosine phosphorylation in psoriatic T cells is modulated by drugs that induce or improve psoriasis.
AU Ockenfels H M; Nussbaum G; Schultewolter T; Mertins K; Wagner S N; Goos M
SO DERMATOLOGY, (1995) 191 (3) 217-25.
Journal code: 9203244. ISSN: 1018-8665.
AB BACKGROUND: The induction of protein tyrosine kinases (PTKs) is known to be a key element in the activation of lymphocytes. OBJECTIVE: Because immunologic mechanisms are important in the pathogenesis of psoriasis, we examined the time course of tyrosine-phosphorylated proteins (p-tyr) as a marker for cellular PTK activity in phytohemagglutinin (PHA)-stimulated T cells of psoriatic patients and healthy controls. METHODS AND RESULTS: PHA-stimulated T cells from both groups expressed peaks of p-tyr after 15 min and 4 h. In T cells from psoriatics, the 15-min peak was smaller but the 4-hour peak reached an enormous maximum, which was 270% higher than the basic p-tyr value. PHA-stimulated T cells were additionally treated with psoriasis-provoking drugs (lithium, chloroquine, propranolol and ethanol) and the two immunosuppressive drugs cyclosporin A and FK 506. Lithium and propranolol were able to increase the p-tyr level after 15 min in PHA-stimulated T cells from psoriatics in contrast to controls. Chloroquine and ethanol did not have a significant effect on T cells of both groups. CsA markedly diminished the phosphorylation of intracellular tyrosines in T cells of psoriatics and controls, whereas FK 506 diminished the p-tyr level in controls only slightly. CONCLUSION: We have characterized important differences in p-tyr phosphorylation activities of psoriatic T cells compared to controls. This could be a hint to explain the known abnormalities of psoriatic T cells.

L24 ANSWER 11 OF 19 MEDLINE on STN
AN 96067795 MEDLINE
TI Liposomal cyclosporine. Characterization of drug incorporation and interbilayer exchange.
AU Ouyang C; Choice E; Holland J; Meloche M; Madden T D
SO TRANSPLANTATION, (1995 Nov 15) 60 (9) 999-1006.
Journal code: 0132144. ISSN: 0041-1337.
AB A number of previous studies have examined the application of liposomes as carriers for the immunosuppressive agent cyclosporine. These studies, however, have generated equivocal results, particularly with regard to the therapeutic properties of such systems. In the present work, we have characterized cyclosporine incorporation into well defined liposomes, large unilamellar vesicles, and have examined the stability of drug association. Contrary to some earlier reports, we show that only modest levels of cyclosporine can be accommodated in the liposomal membrane and that the extent of drug incorporation is greatly reduced as the bilayer cholesterol content is increased. Furthermore, we demonstrate that cyclosporine, despite its hydrophobic character, can rapidly

exchange between vesicles. This raises the possibility that, after i.v. administration, drug migration to other blood components might negate the potential benefits arising from liposomal delivery. In a companion paper, therefore (Choice et al., Transplantation, 1995, this issue), we have followed the pharmacokinetics and biodistribution of liposomal cyclosporine in a study that examined the behavior of both the drug and the liposomal carrier.

L24 ANSWER 12 OF 19 MEDLINE on STN
AN 96007574 MEDLINE
TI Anaphylactoid reactions in children receiving high-dose intravenous cyclosporine for reversal of tumor resistance: the causative role of improper dissolution of Cremophor EL.
AU Theis J G; Liau-Chu M; Chan H S; Doyle J; Greenberg M L; Koren G
SO JOURNAL OF CLINICAL ONCOLOGY, (1995 Oct) 13 (10) 2508-16.
Journal code: 8309333. ISSN: 0732-183X.
AB PURPOSE: An unusually high incidence of anaphylactoid reactions was observed during a phase I/II trial of high-dose intravenous cyclosporine (CsA) therapy to attenuate tumor multidrug resistance (MDR). Five of 21 children experienced severe anaphylactoid reactions shortly after initiation of the first or second CsA infusion. We hypothesized that improper dissolution of the vehicle Cremophor EL may have been a cause for these anaphylactoid reactions. METHODS: All nurses who had administered intravenous CsA were interviewed regarding their technique of preparing the infusion and the occurrence of an anaphylactoid reaction. The responses were statistically analyzed. The effect of various mixing techniques on the distribution of Cremophor EL in the infusion was experimentally evaluated. Different mixing techniques were used to assess their effect on the distribution of Cremophor EL in the solution. RESULTS: Analysis of the preparation techniques of the CsA infusion showed significant correlation between suboptimal mixing of CsA by nurses and the occurrence of anaphylactoid reactions (P = .02). Experimental simulation showed that suboptimal mixing results in an uneven distribution of Cremophor EL, which subsequently sinks to the bottom of the vial. CONCLUSION: Improper mixing of high-dose CsA infusions causes nonsolubilized Cremophor EL to sink to the outflow area of the bottle. An initial bolus infusion of highly concentrated Cremophor EL may produce an anaphylactoid-like response. This mechanism of toxicity is important to recognize, because it is easily preventable by proper preparation of the infusion, thus reducing the incidence of potentially life-threatening anaphylactoid reactions.

L24 ANSWER 13 OF 19 MEDLINE on STN
AN 95138836 MEDLINE
TI Cyclosporin increases the CNS sensitivity to the hypnotic effect of phenobarbitone but not ethanol in rats.
AU Hoffman A; Habib G; Gilhar D; Zohar H
SO JOURNAL OF PHARMACY AND PHARMACOLOGY, (1994 Sep) 46 (9) 760-4.
Journal code: 0376363. ISSN: 0022-3573.
AB The purpose of this investigation was to determine whether repetitive administration of cyclosporin affects the pharmacodynamics of phenobarbitone- and ethanol-induced anaesthesia. Sabra male rats received either cyclosporin (50 mg kg-1 day-1, i.m.) for four days, or the same volume of the vehicle. Two hours after the last cyclosporin dose, phenobarbitone or ethanol solutions were infused intravenously at a constant rate until the onset of

anaesthesia. Repetitive treatment with cyclosporin increased the CNS sensitivity to the hypnotic action of phenobarbitone. This was evidenced by the lower CSF phenobarbitone concentration, at the onset of the hypnotic effect, in the cyclosporin-treated group vs control values (115 +/- 4 vs 93 +/- 7 mg L-1, P = 0.01). However, the same pretreatment had no apparent effect on the pharmacodynamics of ethanol-induced sleep. It is suggested that anaesthesiologists must be alert to the possible increase in brain sensitivity when placing cyclosporin patients under anaesthesia with barbiturates.

L24 ANSWER 14 OF 19 MEDLINE on STN
AN 94157742 MEDLINE
TI Potential neurotoxicity of the solvent vehicle for cyclosporine.
AU Windebank A J; Blexrud M D; de Groen P C
SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1994 Feb) 268 (2) 1051-6.
Journal code: 0376362. ISSN: 0022-3565.
AB Nervous system complications resulting from i.v. administration of cyclosporine (CS) are especially frequent in liver transplant recipients. Because CS is insoluble in water, the i.v. preparation is formulated in a polyoxyethylated castor oil and ethyl alcohol. Rat dorsal root ganglion neurons exposed in vitro to the i.v. preparation exhibited axonal swelling and degeneration. No effect of CS (dissolved directly in serum) was seen on testing individual components of the i.v. solution. However, 0.1% polyoxyethylated castor oil (volume of solute/volume of solvent) produced axonal swelling and degeneration and 0.001% polyoxyethylated castor oil produced demyelination in vitro. Polyoxyethylated castor oil is manufactured by reacting castor oil with ethylene oxide, and we speculate that residual ethylene oxide or a polymerization product may be responsible for the in vitro neurotoxicity. Although little is known about the pharmacokinetics of polyoxyethylated castor oil, plasma levels of 0.001 to 0.01% polyoxyethylated castor oil (volume of solute/volume of solvent) are probably achieved with therapeutic doses of the i.v. CS preparation.

L24 ANSWER 15 OF 19 MEDLINE on STN
AN 94066419 MEDLINE
TI The effect of cyclosporine A dissolved in chremofore or in ethanol and of cortisone on the arterial release of prostacyclin.
AU Brunkwall J; Bergqvist D
SO JOURNAL OF SURGICAL RESEARCH, (1993 Dec) 55 (6) 622-7.
Journal code: 0376340. ISSN: 0022-4804.
AB Cyclosporine A has been suggested to increase thromboembolic complications after renal transplantation. Therefore, the effect of cyclosporine A (at the clinically used dose of 10 mg/kg) dissolved in either chremofore or ethanol on rabbit vascular prostacyclin release was investigated in an ex vivo perfusion system. The animals received the drugs intravenously either as a single injection the day before operation or daily for 1 month prior to operation. Rabbits given cyclosporine A dissolved in chremofore released less prostacyclin than controls, both after a single injection and after 1 month of daily injections. The vehicle chremofore also gave a significantly lower release of prostacyclin than the control. The response to arachidonic acid with increased release was equal in all groups. Cyclosporine A dissolved in ethanol did not alter the initial release, and ethanol alone did not influence the prostacyclin release. Cortisone depressed the

vascular prostacyclin release after daily injections for 1 month, but did not after only one injection. Cyclosporine A dissolved in chremofore and cortisone given in combination did not result in an additive reduction. These findings indicate that the intravenous administration of cyclosporine A dissolved in chremofore, but not that dissolved in ethanol, as well as cortisone, might decrease the vascular defense against thrombus formation. The action of these substances is higher up in the arachidonic acid cascade than the cyclooxygenase level.

L24 ANSWER 16 OF 19 MEDLINE on STN
AN 94003016 MEDLINE
TI Effects of cyclosporine and its metabolites in the isolated perfused rat kidney.
AU Roby K A; Shaw L M
SO JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY, (1993 Aug) 4 (2) 168-77.
Journal code: 9013836. ISSN: 1046-6673.
AB The isolated perfused rat kidney (IPK) was used to study the acute effects of cyclosporin A (CsA) and its metabolites (M1, M17, M18, M21 and M-COOH). GFR, renal vascular resistance, and sodium, potassium and water reabsorption were measured before and after the addition of CsA/metabolites/vehicles. There was no difference in CsA effect (mild decrease in GFR and increase in renal vascular resistance with the inclusion of plasma (10 mL) or whole blood (20 mL) in the albumin perfusate (120 mL). Intralipid was used as the vehicle for CsA and the metabolites because methanol, ethanol, and Cremophor had significant effects on GFR. Intralipid enhanced the effect of CsA 25-fold, giving CsA dose responses comparable to those of human kidneys. This enhanced effect with intralipid was due to vasoconstriction, not vascular obstruction, and was apparently specific to CsA (no enhancement of norepinephrine with Intralipid). The primary metabolites (M1, M17, and M21) caused decreases in GFR comparable to or slightly less than those caused by CsA. The secondary metabolites (M18 and M-COOH) caused more modest declines in GFR. Cyclosporine metabolite levels in patient blood often greatly exceed levels of the parent drug; these studies suggest that the metabolites may contribute significantly to CsA nephrotoxicity in patients.

L24 ANSWER 17 OF 19 MEDLINE on STN
AN 93358503 MEDLINE
TI Evaluation of evacuated blood-collection tubes: effects of three types of polymeric separators on therapeutic drug-monitoring specimens.
AU Landt M; Smith C H; Hortin G L
SO CLINICAL CHEMISTRY, (1993 Aug) 39 (8) 1712-7.
Journal code: 9421549. ISSN: 0009-9147.
AB The potential of three types of separator materials found in conventional blood-collection tubes for interference in therapeutic drug measurements was assessed. None of the separators (based on acrylic, silicone, or polyester polymers) had any significant effect on the concentrations of seven drugs (theophylline, digoxin, phenytoin, phenobarbital, gentamicin, ethanol, and cyclosporine) in blood specimens that were processed and analyzed promptly. Storage of specimens for 24 h resulted in an average 2.4% increase in theophylline values in specimens collected in tubes with the acrylic separator (P = 0.024); an average 8.1% decrease in phenytoin in

specimens collected in tubes with the polyester-based separator (P < 0.001); and an average 4.2% decrease in phenobarbital in specimens collected in tubes with the polyester-based separator (P = 0.02). All other drug concentrations were not significantly affected. A small decrease in phenytoin (7.9%; P < 0.01) was seen when the specimen volume in 7-mL tubes containing polyester-based separator was reduced to 1.0 mL; all other drug concentrations were unaffected by partial filling of tubes. Paired blood specimens from pediatric patients, when collected in plain tubes and tubes containing acrylic separator, yielded no significant differences for theophylline, digoxin, tobramycin, phenytoin, or phenobarbital concentrations. The three commercially available separators had only small effects on therapeutic drug concentrations, and a newly developed separator based on an acrylic resin was suitably inert.

L24 ANSWER 18 OF 19 MEDLINE on STN
AN 92174256 MEDLINE
TI The effect of alkanols on Ca2+ transport in brain mitochondria.
AU Rottenberg H; Marbach M
SO CELL CALCIUM, (1992 Jan) 13 (1) 41-7.
Journal code: 8006226. ISSN: 0143-4160.
AB Ethanol stimulates the Na(+)-dependent Ca2+ efflux in brain mitochondria and inhibits the Na(+)-independent Ca(2+)-efflux. Here, we studied the effects of n-alkanols on the various Ca2+ transport processes in brain mitochondria. Only short-chain alcohols (i.e. methanol, ethanol and propanol) stimulated Na+/Ca2+ exchange. The inhibition of H+/Ca2+ exchange was significant only with ethanol. Short-chain alcohols inhibit while long-chain alcohols activate the cyclosporin-sensitive Ca(2+)-efflux. These data suggest that the mechanism of the alkanols' effects on Na+/Ca2+ exchange, H+/Ca2+ exchange and the cyclosporin sensitive pore are entirely different. Alkanols have no effect on the electrogenic Ca2+ uniporter. Ethanol did not affect the apparent K0.5 for Na+ (7.5 mM) of the Na+/Ca2+ exchange. Similarly, the magnitude of the effect of ethanol did not depend on matrix Ca2+ concentration, suggesting that short-chain alkanols do not stimulate the rate of Na+/Ca2+ exchange by increasing the affinity of the carrier to Ca2+in or Na+out. High concentrations of K+, Mg2+ and Ca2+ enhanced the ethanol effect. It is possible that high surface potential attenuates the effect of ethanol. It is suggested that ethanol stimulation of Na+/Ca2+ exchange depends on the modulation of the surface dielectric constant.

L24 ANSWER 19 OF 19 MEDLINE on STN
AN 92087082 MEDLINE
TI A biochemical and 31P-NMR investigation of the effect of FK 506 and cyclosporine pretreatment on immobilized hepatocytes perifused with ethanol.
AU Farghali H; Sakr M; Gasbarrini A; Williams D S; Dowd S R; Ho C; Van Thiel D H
SO TRANSPLANTATION PROCEEDINGS, (1991 Dec) 23 (6) 2805-8.
Journal code: 0243532. ISSN: 0041-1345.

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